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(74) Agents: **BASTIAN, Kevin, L.** et al.; Townsend and Townsend and Crew LLP, Two Embarcadero Center, Eighth Floor, San Francisco, CA 94111 (US).

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(71) Applicant: **EOS BIOTECHNOLOGY, INC.** [US/US]; 225A Gateway Boulevard, South San Francisco, CA 94080 (US).

(72) Inventors: **AFAR, Daniel, E., H.**; 435 Visitacion Avenue, Brisbane, CA 94005 (US). **AGUS, David**; 522 North Crescent Drive, Beverly Hills, CA 90210 (US). **MACK, David, H.**; 2076 Monterey Avenue, Menlo Park, CA 94025 (US).



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(54) Title: METHODS OF DIAGNOSIS AND TREATMENT OF ANDROGEN-DEPENDENT PROSTATE CANCER, PROSTATE CANCER UNDERGOING ANDROGEN-WITHDRAWAL, AND ANDROGEN-INDEPENDENT PROSTATE CANCER

(57) Abstract: Described herein are genes whose expression are up-regulated or down-regulated in prostate cancer. Also described are such genes whose expression is further up-regulated or down-regulated in drug-resistant prostate cancer cells. Related methods and compositions that can be used for diagnosis and treatment of prostate cancer are disclosed. Also described herein are methods that can be used to identify modulators of prostate cancer.

METHODS OF DIAGNOSIS AND TREATMENT OF ANDROGEN-DEPENDENT
PROSTATE CANCER, PROSTATE CANCER UNDERGOING ANDROGEN
WITHDRAWAL, AND ANDROGEN-INDEPENDENT PROSTATE CANCER

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CROSS-REFERENCES TO RELATED APPLICATIONS

This application claims priority from the following applications: USSN 60/295,917,
filed June 4, 2001, USSN 60/368,689, filed March 29, 2002; USSN 60/350,666, filed
November 13, 2001; and USSN 60/372,246, filed April 12, 2002; each of which is
10 incorporated herein by reference in its entirety.

FIELD OF THE INVENTION

The invention relates to the identification of nucleic acid and protein expression
profiles and nucleic acids, products, and antibodies thereto that are involved in prostate
15 cancer; and to the use of such expression profiles and compositions in the diagnosis,
prognosis, and therapy of prostate cancer. The invention further relates to methods for
identifying and using agents and/or targets that inhibit prostate cancer.

BACKGROUND OF THE INVENTION

20 Prostate cancer is the most frequently diagnosed cancer and the second leading cause
of male cancer death in North America and northern Europe. Early detection of prostate
cancer using a serum test for prostate-specific antigen (PSA) has dramatically improved the
treatment of the disease (Oesterling (1992) J. Am. Med. Assoc. 267:2236-2238). Treatment
of prostate cancer consists largely of surgical prostatectomy, radiation therapy, androgen
25 ablation therapy and chemotherapy. Although many prostate cancer patients are effectively
treated, the current therapies can all induce serious side effects which diminish quality of life.
Patients who present with metastatic disease are most often treated with androgen-ablation
therapy. Hormone blockade results in significant regression of the tumor. However, this
treatment rarely cures the patient and invariably results in progression to androgen-

independent disease, which is incurable. Afrin and Stuart (1994) J.S.C. Med. Assoc. 90:231-236.

The identification of novel therapeutic targets and diagnostic markers is essential for improving the current treatment of prostate cancer patients. Recent advances in molecular medicine have increased the interest in tumor-specific cell surface antigens that could serve as targets for various immunotherapeutic or small molecule strategies. Antigens suitable for immunotherapeutic strategies should be highly expressed in cancer tissues and ideally not expressed in normal adult tissues. Expression in tissues that are dispensable for life, however, may be tolerated. Examples of such antigens include Her2/neu and the B-cell antigen CD20. Humanized monoclonal antibodies directed to Her2/neu (Herceptin) are currently in use for the treatment of metastatic breast cancer. Ross and Fletcher (1998) Stem Cells 16:413-428. Similarly, anti-CD20 monoclonal antibodies (Rituxin) are used to effectively treat non-Hodgkin's lymphoma. Maloney, et al. (1997) Blood 90:2188-2195; Leget and Czuczman (1998) Curr. Opin. Oncol. 10:548-551.

Several potential immunotherapeutic targets have been identified for prostate cancer. They include prostate-specific membrane antigen (PSMA) (Israeli, et al. (1993) Cancer Res. 53:227-230), prostate stem cell antigen (PSCA; Reiter, et al. (1998) Proc. Natl. Acad. Sci. USA 95:1735-1740), and serpentine transmembrane epithelial antigen of the prostate (STEAP; Hubert, et al. (1999) Proc. Natl. Acad. Sci. USA 96:14529-14534). PSMA is a type II transmembrane hydrolase with significant homology to a rat neuropeptidase (Carter, et al. (1996) Proc. Natl. Acad. Sci. USA 93:749-753). Antibodies directed towards PSMA are currently being used to detect metastasized prostate cancer as the Proscint Scan (Sodee, et al. (1996) Clin. Nucl. Med. 21:759-767) and are also being evaluated for treatment of advanced disease (Gregorakis, et al. (1998) Semin. Urol. Oncol. 16:2-12; Liu, et al. (1998) Cancer Res. 58:4055-4060; Murphy, et al. (1998) J. Urol. 160:2396-2401). In a study on bone metastasis of prostate cancer, only 8 out of 18 patient samples expressed PSMA (Silver, et al. (1997) Clin. Cancer Res. 3:81-85). Therefore, it is clear that other targets need to be identified to manage metastasized disease. PSCA is a member of the Thy-1/Ly-6 family of glycosylphosphatidylinositol-linked plasma membrane proteins (Reiter, et al. (1998) Proc. Natl. Acad. Sci. USA 95:1735-1740). Immunohistochemical data shows that PSCA is up-regulated in the majority of prostate cancer epithelia and is also detected in bone metastasis (Gu, et al. (2000) Oncogene 19:1288-1296). Recent work shows that antibodies directed to

PSCA can prevent metastatic spread of prostate cancer in a mouse model (Saffran, et al. (2001) Proc. Natl. Acad. Sci. USA 98:2658-2663). STEAP is a multi-transmembrane prostate-specific protein that may function as a channel or transporter protein (Hubert, et al. (1999) Proc. Natl. Acad. Sci. USA 96:14529-14534). Its protein expression is specific to the basolateral membranes of normal prostate and prostate cancer epithelia. STEAP expression was most highly concentrated at cell-cell boundaries, implying a potential function in intercellular communication. Therapeutic monoclonal antibodies have so far not been reported for STEAP.

10 SUMMARY OF THE INVENTION

The present invention therefore provides nucleotide sequences of genes that are up- and down-regulated in androgen-independent prostate cancer cells or prostate cells undergoing androgen withdrawal. Such genes are useful for diagnostic purposes, and also as targets for screening for therapeutic compounds that modulate prostate cancer, such as hormones or antibodies. Other aspects of the invention will become apparent to the skilled artisan by the following description of the invention.

In one aspect, the present invention provides a method of detecting an androgen independent prostate cancer-associated transcript in a cell from a patient, the method comprising contacting a biological sample from the patient with a polynucleotide that selectively hybridizes to nucleic acid molecule comprising a sequence at least 80% identical to a sequence as shown in Tables 1A-4.

In one embodiment, the present invention provides a method of determining the level of a prostate cancer associated transcript in a cell from a patient.

In one embodiment, the present invention provides a method of detecting a prostate cancer-associated transcript in a cell from a patient, the method comprising contacting a biological sample from the patient with a polynucleotide that selectively hybridizes to a sequence at least 80% identical to a sequence as shown in Tables 1A-4.

In various embodiments, the polynucleotide selectively hybridizes to a sequence at least 95% identical to a sequence as shown in Tables 1A-4; the polynucleotide comprises a sequence as shown in Tables 1A-4; the biological sample is a tissue sample; the biological sample comprises isolated nucleic acids, e.g., mRNA; the polynucleotide is labeled, e.g., with a fluorescent label; the polynucleotide is immobilized on a solid surface; the patient is

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undergoing a therapeutic regimen to treat prostate cancer; the patient is suspected of having metastatic prostate cancer; the patient is a human; the patient is suspected of having a taxol-resistant cancer; or the prostate cancer associated transcript is mRNA.

5 In other embodiments, the method further comprises the step of amplifying nucleic acids before the step of contacting the biological sample with the polynucleotide.

• In another aspect, the present invention provides a method of monitoring the efficacy of a therapeutic treatment of prostate cancer, the method comprising the steps of: (i) providing a biological sample from a patient undergoing the therapeutic treatment; and (ii) determining the level of a prostate cancer-associated transcript in the biological sample by
10 contacting the biological sample with a polynucleotide that selectively hybridizes to a sequence at least 80% identical to a sequence as shown in Tables 1A-4, thereby monitoring the efficacy of the therapy. In a further embodiment, the patient has metastatic prostate cancer. In a further embodiment, the patient has a drug resistant (e.g., taxol resistant) form of prostate cancer.

15 In one embodiment, the method further comprises the step of: (iii) comparing the level of the prostate cancer-associated transcript to a level of the prostate cancer-associated transcript in a biological sample from the patient prior to, or earlier in, the therapeutic treatment.

20 Additionally, provided herein is a method of evaluating the effect of a candidate prostate cancer drug comprising administering the drug to a patient and removing a cell sample from the patient. The expression profile of the cell is then determined. This method may further comprise comparing the expression profile to an expression profile of a healthy individual. In a preferred embodiment, said expression profile includes a gene of Tables 1A-4.

25 In one aspect, the present invention provides an isolated nucleic acid molecule consisting of a polynucleotide sequence as shown in Tables 1A-4.

In one embodiment, an expression vector or cell comprises the isolated nucleic acid.

In one aspect, the present invention provides an isolated polypeptide which is encoded by a nucleic acid molecule having polynucleotide sequence as shown in Tables 1A-4.

30 In another aspect, the present invention provides an antibody that specifically binds to an isolated polypeptide which is encoded by a nucleic acid molecule having polynucleotide sequence as shown in Tables 1A-4.

In certain embodiments, the antibody is conjugated to an effector component, e.g., a fluorescent label, a radioisotope or a cytotoxic chemical; the antibody is an antibody fragment; or the antibody is humanized.

In one aspect, the present invention provides a method of detecting a prostate cancer cell in a biological sample from a patient, the method comprising contacting the biological sample with an antibody as described herein.

In another aspect, the present invention provides a method of detecting antibodies specific to prostate cancer in a patient, the method comprising contacting a biological sample from the patient with a polypeptide encoded by a nucleic acid comprising a sequence from Tables 1A-4.

In another aspect, the present invention provides a method for identifying a compound that modulates a prostate cancer-associated polypeptide, the method comprising the steps of: a) contacting the compound with a prostate cancer-associated polypeptide, the polypeptide encoded by a polynucleotide that selectively hybridizes to a sequence at least 80% identical to a sequence as shown in Tables 1A-4; and b) determining the functional effect of the compound upon the polypeptide.

In one embodiment, the functional effect is a physical effect, an enzymatic effect, or a chemical effect.

In one embodiment, the polypeptide is expressed in a eukaryotic host cell or cell membrane. In another embodiment, the polypeptide is recombinant.

In one embodiment, the functional effect is determined by measuring ligand binding to the polypeptide.

In another aspect, the present invention provides a method of inhibiting proliferation of a prostate cancer-associated cell to treat prostate cancer in a patient, the method comprising the step of administering to the subject a therapeutically effective amount of a compound identified as described herein.

In one embodiment, the compound is an antibody.

In another aspect, the present invention provides a drug screening assay comprising the steps of: a) administering a test compound to a mammal having prostate cancer or to a cell sample isolated therefrom; b) comparing the level of gene expression of a polynucleotide that selectively hybridizes to a sequence at least 80% identical to a sequence as shown in Tables 1A-4 in a treated cell or mammal with the level of gene expression of the

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polynucleotide in a control cell sample or mammal, wherein a test compound that modulates the level of expression of the polynucleotide is a candidate for the treatment of prostate cancer.

5 In one embodiment, the control is a mammal with prostate cancer or a cell sample therefrom that has not been treated with the test compound. In another embodiment, the control is a normal cell or mammal.

In one embodiment, the test compound is administered in varying amounts or concentrations. In another embodiment, the test compound is administered for varying time periods. In another embodiment, the comparison can occur after addition or removal of the
10 drug candidate.

In one embodiment, the levels of a plurality of polynucleotides that selectively hybridize to a sequence at least 80% identical to a sequence as shown in Tables 1A-4 are individually compared to their respective levels in a control cell sample or mammal. In a preferred embodiment the plurality of polynucleotides is from three to ten.

15 In another aspect, the present invention provides a method for treating a mammal having prostate cancer comprising administering a compound identified by the assay described herein.

In another aspect, the present invention provides a pharmaceutical composition for treating a mammal having prostate cancer, the composition comprising a compound
20 identified by the assay described herein and a physiologically acceptable excipient.

In one aspect, the present invention provides a method of screening drug candidates by providing a cell expressing a gene that is up- and down-regulated as in a prostate cancer. In one embodiment, a gene is selected from Tables 1A-4. The method further includes adding a drug candidate to the cell and determining the effect of the drug candidate on the
25 expression of the expression profile gene.

In one embodiment, the method of screening drug candidates includes comparing the level of expression in the absence of the drug candidate to the level of expression in the presence of the drug candidate, wherein the concentration of the drug candidate can vary when present, and wherein the comparison can occur after addition or removal of the drug
30 candidate. In a preferred embodiment, the cell expresses at least two expression profile genes. The profile genes may show an increase or decrease.

Also provided is a method of evaluating the effect of a candidate prostate cancer drug comprising administering the drug to a transgenic animal expressing or over-expressing the prostate cancer modulatory protein, or an animal lacking the prostate cancer modulatory protein, for example as a result of a gene knockout.

5 Moreover, provided herein is a biochip comprising one or more nucleic acid segments of Tables 1A-4, wherein the biochip comprises fewer than 1000 nucleic acid probes. Preferably, at least two nucleic acid segments are included. More preferably, at least three nucleic acid segments are included.

10 Furthermore, a method of diagnosing a disorder associated with prostate cancer is provided. The method comprises determining the expression of a gene of Tables 1A-4, in a first tissue type of a first individual, and comparing the distribution to the expression of the gene from a second normal tissue type from the first individual or a second unaffected individual. A difference in the expression indicates that the first individual has a disorder associated with prostate cancer.

15 In a further embodiment, the biochip also includes a polynucleotide sequence of a gene that is not up- and down-regulated in prostate cancer.

20 In one embodiment a method for screening for a bioactive agent capable of interfering with the binding of a prostate cancer modulating protein (prostate cancer modulatory protein) or a fragment thereof and an antibody which binds to said prostate cancer modulatory protein or fragment thereof. In a preferred embodiment, the method comprises combining a prostate cancer modulatory protein or fragment thereof, a candidate bioactive agent and an antibody which binds to said prostate cancer modulatory protein or fragment thereof. The method further includes determining the binding of said prostate cancer modulatory protein or fragment thereof and said antibody. Wherein there is a change in binding, an agent is
25 identified as an interfering agent. The interfering agent can be an agonist or an antagonist. Preferably, the agent inhibits prostate cancer.

30 Also provided herein are methods of eliciting an immune response in an individual. In one embodiment a method provided herein comprises administering to an individual a composition comprising a prostate cancer modulating protein, or a fragment thereof. In another embodiment, the protein is encoded by a nucleic acid selected from those of Tables 1A-4.

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Further provided herein are compositions capable of eliciting an immune response in an individual. In one embodiment, a composition provided herein comprises a prostate cancer modulating protein, preferably encoded by a nucleic acid of Tables 1A-4, or a fragment thereof, and a pharmaceutically acceptable carrier. In another embodiment, said composition comprises a nucleic acid comprising a sequence encoding a prostate cancer modulating protein, preferably selected from the nucleic acids of Tables 1A-4 and a pharmaceutically acceptable carrier.

Also provided are methods of neutralizing the effect of a prostate cancer protein, or a fragment thereof, comprising contacting an agent specific for said protein with said protein in an amount sufficient to effect neutralization. In another embodiment, the protein is encoded by a nucleic acid selected from those of Tables 1A-4. In another aspect of the invention, a method of treating an individual for prostate cancer is provided. In one embodiment, the method comprises administering to said individual an inhibitor of a prostate cancer modulating protein. In another embodiment, the method comprises administering to a patient having prostate cancer an antibody to a prostate cancer modulating protein conjugated to a therapeutic moiety. Such a therapeutic moiety can be a cytotoxic agent or a radioisotope.

DETAILED DESCRIPTION OF THE INVENTION

In accordance with the objects outlined above, the present invention provides novel methods for diagnosis and evaluation of androgen-dependent prostate cells (malignant or non-malignant), prostate cells undergoing androgen withdrawal, and androgen-independent prostate cancer, as well as methods for treating androgen-dependent prostate cells (malignant or non-malignant), prostate cancer undergoing androgen withdrawal, and androgen-independent prostate cancer. The current Specification incorporates the text of USSN 09/976,858, filed October 12, 2001, USSN 60/295,917, filed June 4, 2001, USSN 60/368,689, filed March 29, 2002; USSN 60/350,666, filed November 13, 2001; and USSN 60/372,246, filed April 12, 2002.

Table 1A provides unigene cluster identification numbers for the nucleotide sequence of genes that exhibit increased or decreased expression in androgen-independent prostate cancer samples. Table 1A also provides an exemplar accession number that provides a nucleotide sequence that is part of the unigene cluster. The expression patterns of the genes of Table 1A can be broadly defined into the following categories:

Genes that are expressed early in the time course, then drop off in expression, and then express again with emergence of androgen-independence (hi-lo-hi pattern in table 1A). Genes that are expressed early in the time course, then drop off in expression, and do not express again with emergence of androgen-independence (hi-lo-lo pattern in 1A). Genes that
5 are not expressed early in the time course, but express only with emergence of androgen-independence (lo-lo-hi pattern in table 1A). Genes that are not expressed early in the time course, but then express as androgen is withdrawn and continue to express with emergence of androgen-independence (lo-hi-hi pattern in table 1A). Genes that are not expressed early in the time course, but then express as androgen is withdrawn and drop off again with
10 emergence of androgen-independence (lo-hi-lo pattern in table 1A).

Tables 2A-C provide unigene cluster identification numbers for the nucleotide sequence of genes that exhibit increased or decreased expression in androgen-dependent prostate cancer, prostate cancer undergoing androgen withdrawal and androgen-independent prostate cancer. Tables 2A-C also provide an exemplar accession number that provides a
15 nucleotide sequence that is part of the unigene cluster. The expression patterns of the genes of Tables 2A-C can be broadly defined into the following 6 categories:

Genes that are expressed early in the time course of androgen withdrawal, then drop off in expression, and then express again with emergence of androgen-independence (hi-lo-lo-hi pattern in Table 2A). Genes that are expressed early in the time course, then drop off in
20 expression immediately after androgen-withdrawal, and do not express again with emergence of androgen-independence (hi-lo-lo-lo pattern in Table 2A). Genes that are expressed early in the time course, then drop off in expression after several days of androgen withdrawal, and do not express again with emergence of androgen-independence (hi-hi-lo-lo pattern in Table 2A). Genes that are not expressed early in the time course, but express only with emergence
25 of androgen-independence (lo-lo-lo-hi pattern in Table 2A). Genes that are not expressed early in the time course, but then express as androgen is withdrawn and continue to express with emergence of androgen-independence (lo-lo-hi-hi pattern in Table 2A). Genes that are not expressed early in the time course, but then express as androgen is withdrawn and drop off again with emergence of androgen-independence (lo-lo-hi-lo pattern in Table 2A).

30

Definitions

The term “androgen ablation therapy” refers to techniques for the removal or destruction of sources of male hormones, such as testosterone. These techniques include, for example, 1) surgical removal of the testicles, 2) medications such as gonadotropin releasing hormone analogs that inhibit testosterone production, or 3) anti-androgenic drugs that block androgen receptors.

The term “androgen-independent prostate cancer protein” or “androgen-independent prostate cancer polynucleotide” or “androgen-independent prostate cancer-associated transcript” refers to nucleic acid and polypeptide polymorphic variants, alleles, mutants, and interspecies homologues that: (1) have a nucleotide sequence that has greater than about 60% nucleotide sequence identity, 65%, 70%, 75%, 80%, 85%, 90%, preferably 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or greater nucleotide sequence identity, preferably over a region of over a region of at least about 25, 50, 100, 200, 500, 1000, or more nucleotides, to a nucleotide sequence of or associated with a unigene cluster of Tables 1A-4; (2) bind to antibodies, e.g., polyclonal antibodies, raised against an immunogen comprising an amino acid sequence encoded by a nucleotide sequence of or associated with a unigene cluster of Tables 1A-4 and conservatively modified variants thereof; (3) specifically hybridize under stringent hybridization conditions to a nucleic acid sequence, or the complement thereof of Tables 1A-4 and conservatively modified variants thereof; or (4) have an amino acid sequence that has greater than about 60% amino acid sequence identity, 65%, 70%, 75%, 80%, 85%, 90%, preferably 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or greater amino sequence identity, preferably over a region of over a region of at least about 25, 50, 100, 200, 500, 1000, or more amino acid, to an amino acid sequence encoded by a nucleotide sequence of or associated with a unigene cluster of Tables 1A-4. These polynucleotides or proteins may also be expressed during a period following androgen withdrawal. A polynucleotide or polypeptide sequence is typically from a mammal including, but not limited to, primate, e.g., human; rodent, e.g., rat, mouse, hamster; cow, pig, horse, sheep, or other mammal. A “prostate cancer polypeptide” and a “prostate cancer polynucleotide,” include both naturally occurring or recombinant forms, and may refer to those polypeptides or polynucleotides which are expressed in prostate proliferative cells.

A “full length” prostate cancer protein or nucleic acid refers to a prostate cancer polypeptide or polynucleotide sequence, or a variant thereof, that contains the elements normally contained in one or more naturally occurring, wild type prostate cancer

polynucleotide or polypeptide sequences. The “full length” may be prior to, or after, various stages of post-translation processing or splicing, including alternative splicing.

“Biological sample” as used herein is a sample of biological tissue or fluid that contains nucleic acids or polypeptides, e.g., of a prostate cancer protein, polynucleotide or transcript. Such samples include, but are not limited to, tissue isolated from primates, e.g.,
5 humans, or rodents, e.g., mice, and rats. Biological samples may also include sections of tissues such as biopsy and autopsy samples, frozen sections taken for histology purposes, blood, plasma, serum, sputum, stool, tears, mucus, hair, skin, etc. Biological samples also include explants and primary and/or transformed cell cultures derived from patient tissues. A
10 biological sample is typically obtained from a eukaryotic organism, most preferably a mammal such as a primate e.g., chimpanzee or human; cow; dog; cat; a rodent, e.g., guinea pig, rat, mouse; rabbit; or a bird; reptile; or fish.

“Providing a biological sample” means to obtain a biological sample for use in methods described in this invention. Most often, this will be done by removing a sample of
15 cells from an animal, but can also be accomplished by using previously isolated cells (e.g., isolated by another person, at another time, and/or for another purpose), by collecting a sample which contains a soluble polypeptide or nucleic acid derived from a prostate cell, or by performing the methods of the invention in vivo. Archival tissues, having treatment or outcome history, will be particularly useful.

20 The terms “identical” or percent “identity,” in the context of two or more nucleic acids or polypeptide sequences, refer to two or more sequences or subsequences that are the same or have a specified percentage of amino acid residues or nucleotides that are the same (i.e., about 60% identity, preferably 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%,
25 96%, 97%, 98%, 99%, or higher identity over a specified region, when compared and aligned for maximum correspondence over a comparison window or designated region) as measured using a BLAST or BLAST 2.0 sequence comparison algorithms with default parameters described below, or by manual alignment and visual inspection (see, e.g., NCBI web site
http://www.ncbi.nlm.nih.gov/BLAST/ or the like). Such sequences are then said to be “substantially identical.” This definition also refers to, or may be applied to, the compliment
30 of a test sequence. The definition also includes sequences that have deletions and/or additions, as well as those that have substitutions, as well as naturally occurring, e.g., polymorphic or allelic variants, and man-made variants. As described below, the preferred

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algorithms can account for gaps and the like. Preferably, identity exists over a region that is at least about 25 amino acids or nucleotides in length, or more preferably over a region that is 50-100 amino acids or nucleotides in length.

For sequence comparison, typically one sequence acts as a reference sequence, to which test sequences are compared. When using a sequence comparison algorithm, test and reference sequences are entered into a computer, subsequence coordinates are designated, if necessary, and sequence algorithm program parameters are designated. Preferably, default program parameters can be used, or alternative parameters can be designated. The sequence comparison algorithm then calculates the percent sequence identities for the test sequences relative to the reference sequence, based on the program parameters.

A "comparison window", as used herein, includes reference to a segment of one of the number of contiguous positions selected from the group consisting typically of from 20 to 600, usually about 50 to about 200, more usually about 100 to about 150 in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned. Methods of alignment of sequences for comparison are well-known in the art. Optimal alignment of sequences for comparison can be conducted, e.g., by the local homology algorithm of Smith and Waterman (1981) Appl. Math. 2:482, by the homology alignment algorithm of Needleman and Wunsch (1970) J. Mol. Biol. 48:443-453, by the search for similarity method of Pearson and Lipman (1988) Proc. Nat'l. Acad. Sci. USA 85:2444-2448, by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group, 575 Science Dr., Madison, WI), or by manual alignment and visual inspection (see, e.g., Ausubel, et al. (eds. 1995 and supplements) Current Protocols in Molecular Biology Lippincott).

Preferred examples of algorithms that are suitable for determining percent sequence identity and sequence similarity include the BLAST and BLAST 2.0 algorithms, which are described in Altschul, et al. (1977) Nuc. Acids Res. 25:3389-3402 and Altschul, et al. (1990) J. Mol. Biol. 215:403-410. BLAST and BLAST 2.0 are used, with the parameters described herein, to determine percent sequence identity for the nucleic acids and proteins of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information (<http://www.ncbi.nlm.nih.gov/>). This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short

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words of length W in the query sequence, which either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul, et al., supra). These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing
5 them. The word hits are extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Cumulative scores are calculated using, e.g., for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always > 0) and N (penalty score for mismatching residues; always < 0). For amino acid sequences, a scoring matrix is used to calculate the cumulative score. Extension of the word
10 hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W , T , and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences)
15 uses as defaults a wordlength (W) of 11, an expectation (E) of 10, $M=5$, $N=-4$ and a comparison of both strands. For amino acid sequences, the BLASTP program uses as defaults a wordlength of 3, and expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff and Henikoff (1989) Proc. Natl. Acad. Sci. USA 89:10915-919) alignments (B)
of 50, expectation (E) of 10, $M=5$, $N=-4$, and a comparison of both strands.

20 The BLAST algorithm also performs a statistical analysis of the similarity between two sequences (see, e.g., Karlin and Altschul (1993) Proc. Nat'l. Acad. Sci. USA 90:5873-5787). One measure of similarity provided by the BLAST algorithm is the smallest sum probability ($P(N)$), which provides an indication of the probability by which a match between two nucleotide or amino acid sequences would occur by chance. For example, a nucleic acid
25 is considered similar to a reference sequence if the smallest sum probability in a comparison of the test nucleic acid to the reference nucleic acid is less than about 0.2, more preferably less than about 0.01, and most preferably less than about 0.001. Log values may be large negative numbers, e.g., 5, 10, 20, 30, 40, 40, 70, 90, 110, 150, 170, etc.

An indication that two nucleic acid sequences or polypeptides are substantially
30 identical is that the polypeptide encoded by the first nucleic acid is immunologically cross reactive with the antibodies raised against the polypeptide encoded by the second nucleic acid, as described below. Thus, a polypeptide is typically substantially identical to a second

polypeptide, e.g., where the two peptides differ only by conservative substitutions. Another indication that two nucleic acid sequences are substantially identical is that the two molecules or their complements hybridize to each other under stringent conditions, as described below. Yet another indication that two nucleic acid sequences are substantially identical is that the same primers can be used to amplify the sequences.

A "host cell" is a naturally occurring cell or a transformed cell that contains an expression vector and supports the replication or expression of the expression vector. Host cells may be cultured cells, explants, cells in vivo, and the like. Host cells may be prokaryotic cells such as *E. coli*, or eukaryotic cells such as yeast, insect, amphibian, or mammalian cells such as CHO, HeLa, and the like (see, e.g., the American Type Culture Collection catalog or web site, www.atcc.org).

The terms "isolated," "purified," or "biologically pure" refer to material that is substantially or essentially free from components that normally accompany it as found in its native state. Purity and homogeneity are typically determined using analytical chemistry techniques such as polyacrylamide gel electrophoresis or high performance liquid chromatography. A protein or nucleic acid that is the predominant species present in a preparation is substantially purified. In particular, an isolated nucleic acid is separated from some open reading frames that naturally flank the gene and encode proteins other than protein encoded by the gene. The term "purified" in some embodiments denotes that a nucleic acid or protein gives rise to essentially one band in an electrophoretic gel. Preferably, it means that the nucleic acid or protein is at least 85% pure, more preferably at least 95% pure, and most preferably at least 99% pure. "Purify" or "purification" in other embodiments means removing at least one contaminant from the composition to be purified. In this sense, purification does not require that the purified compound be homogenous, e.g., 100% pure.

The terms "polypeptide," "peptide," and "protein" are used interchangeably herein to refer to a polymer of amino acid residues. The terms apply to amino acid polymers in which one or more amino acid residue is an artificial chemical mimetic of a corresponding naturally occurring amino acid, as well as to naturally occurring amino acid polymers, those containing modified residues, and non-naturally occurring amino acid polymer. Certain diagnostic methods may evaluate secreted or breakdown products present only because the producing cell is present, and would otherwise be absent in a normal individual.

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The term "amino acid" refers to naturally occurring and synthetic amino acids, as well as amino acid analogs and amino acid mimetics that function similarly to the naturally occurring amino acids. Naturally occurring amino acids are those encoded by the genetic code, as well as those amino acids that are later modified, e.g., hydroxyproline, γ -carboxyglutamate, and O-phosphoserine. Amino acid analogs refers to compounds that have the same basic chemical structure as a naturally occurring amino acid, e.g., an α carbon that is bound to a hydrogen, a carboxyl group, an amino group, and an R group, e.g., homoserine, norleucine, methionine sulfoxide, methionine methyl sulfonium. Such analogs may have modified R groups (e.g., norleucine) or modified peptide backbones, but retain the same basic chemical structure as a naturally occurring amino acid. Amino acid mimetics refers to chemical compounds that have a structure that is different from the general chemical structure of an amino acid, but that functions similarly to a naturally occurring amino acid.

Amino acids may be referred to herein by either their commonly known three letter symbols or by the one-letter symbols recommended by the IUPAC-IUB Biochemical Nomenclature Commission. Nucleotides, likewise, may be referred to by their commonly accepted single-letter codes.

"Conservatively modified variants" applies to both amino acid and nucleic acid sequences. With respect to particular nucleic acid sequences, conservatively modified variants refers to those nucleic acids which encode identical or essentially identical amino acid sequences, or where the nucleic acid does not encode an amino acid sequence, to essentially identical or associated, e.g., naturally contiguous, sequences. Because of the degeneracy of the genetic code, a large number of functionally identical nucleic acids encode most proteins. For instance, the codons GCA, GCC, GCG, and GCU encode the amino acid alanine. Thus, at every position where an alanine is specified by a codon, the codon can be altered to another of the corresponding codons described without altering the encoded polypeptide. Such nucleic acid variations are "silent variations," which are one species of conservatively modified variations. Every nucleic acid sequence herein which encodes a polypeptide also describes silent variations of the nucleic acid. One of skill will recognize that in certain contexts each codon in a nucleic acid (except AUG, which is ordinarily the only codon for methionine, and TGG, which is ordinarily the only codon for tryptophan) can be modified to yield a functionally identical molecule. Accordingly, often silent variations of

a nucleic acid which encodes a polypeptide is implicit in a described sequence with respect to the expression product, but not with respect to actual probe sequences.

As to amino acid sequences, one of skill will recognize that individual substitutions, deletions or additions to a nucleic acid, peptide, polypeptide, or protein sequence which
5 alters, adds or deletes a single amino acid or a small percentage of amino acids in the encoded sequence is a "conservatively modified variant" where the alteration results in the substitution of an amino acid with a chemically similar amino acid. Conservative substitutions providing functionally similar amino acids are well known in the art. Such conservatively modified variants are in addition to and do not exclude polymorphic variants, interspecies homologs,
10 and alleles of the invention, typically conservative substitutions for one another: 1) Alanine (A), Glycine (G); 2) Aspartic acid (D), Glutamic acid (E); 3) Asparagine (N), Glutamine (Q); 4) Arginine (R), Lysine (K); 5) Isoleucine (I), Leucine (L), Methionine (M), Valine (V); 6) Phenylalanine (F), Tyrosine (Y), Tryptophan (W); 7) Serine (S), Threonine (T); and 8) Cysteine (C), Methionine (M) (see, e.g., Creighton (1984) Proteins Freeman).

15 Macromolecular structures such as polypeptide structures can be described in terms of various levels of organization. For a general discussion of this organization, see, e.g., Alberts, et al. (2001) Molecular Biology of the Cell (4th ed.) and Cantor and Schimmel (1980) Biophysical Chemistry Part I: The Conformation of Biological Macromolecules Freeman. "Primary structure" refers to the amino acid sequence of a particular peptide.
20 "Secondary structure" refers to locally ordered, three dimensional structures within a polypeptide. These structures are commonly known as domains. Domains are portions of a polypeptide that often form a compact unit of the polypeptide and are typically 25 to approximately 500 amino acids long. Typical domains are made up of sections of lesser organization such as stretches of β -sheet and α -helices. "Tertiary structure" refers to the
25 complete three dimensional structure of a polypeptide monomer. "Quaternary structure" refers to the three dimensional structure formed, usually by the noncovalent association of independent tertiary units. Anisotropic terms are also known as energy terms.

"Nucleic acid" or "oligonucleotide" or "polynucleotide" or grammatical equivalents used herein means at least two nucleotides covalently linked together. Oligonucleotides are
30 typically from about 5, 6, 7, 8, 9, 10, 12, 15, 25, 30, 40, 50 or more nucleotides in length, up to about 100 nucleotides in length. Nucleic acids and polynucleotides are a polymers of virtually any length, including longer lengths, e.g., 200, 300, 500, 1000, 2000, 3000, 5000,

- 7000, 10,000, etc. A nucleic acid of the present invention will generally contain phosphodiester bonds, although in some cases, nucleic acid analogs are included that may have alternate backbones, comprising, e.g., phosphoramidate, phosphorothioate, phosphorodithioate, or O-methylphosphoroamidite linkages (see Eckstein (1992) Oligonucleotides and Analogues: A Practical Approach, Oxford University Press); and peptide nucleic acid backbones and linkages. Other analog nucleic acids include those with positive backbones; non-ionic backbones, and non-ribose backbones, including those described in U.S. Patent Nos. 5,235,033 and 5,034,506, and Chapters 6 and 7, ASC Symposium Series 580, Sanghvi and Cook (eds. 1994) Carbohydrate Modifications in Antisense Research ACS Symposium Series 580. Nucleic acids containing one or more carbocyclic sugars are also included within one definition of nucleic acids. Modifications of the ribose-phosphate backbone may be done for a variety of reasons, e.g., to increase the stability and half-life of such molecules in physiological environments or as probes on a biochip. Mixtures of naturally occurring nucleic acids and analogs can be made; alternatively, mixtures of different nucleic acid analogs, and mixtures of naturally occurring nucleic acids and analogs may be made.

- A variety of references disclose such nucleic acid analogs, including, for example, phosphoramidate (Beaucage, et al. (1993) Tetrahedron 49(10):1925-1963 and references therein; Letsinger (1970) J. Org. Chem. 35:3800-3803; Sprinzl, et al. (1977) Eur. J. Biochem. 81:579-589; Letsinger, et al. (1986) Nucl. Acids Res. 14:3487-499; Sawai, et al (1984) Chem. Lett. 805, Letsinger, et al. (1988) J. Am. Chem. Soc. 110:4470-4471; and Pauwels, et al. (1986) Chemica Scripta 26:141-149), phosphorothioate (Mag, et al. (1991) Nucleic Acids Res. 19:1437-441; and U.S. Patent No. 5,644,048), phosphorodithioate (Briu, et al. (1989) J. Am. Chem. Soc. 111:2321-xxx, O-methylphosphoroamidite linkages (see Eckstein (1992) Oligonucleotides and Analogues: A Practical Approach Oxford University Press), and peptide nucleic acid backbones and linkages (see Egholm (1992) J. Am. Chem. Soc. 114:1895-1897; Meier, et al. (1992) Chem. Int. Ed. Engl. 31:1008-1010; Nielsen (1993) Nature 365:566-568; Carlsson, et al. (1996) Nature 380:207, each of which is incorporated by reference). Other analog nucleic acids include those with positive backbones (Denpcy, et al. (1995) Proc. Natl. Acad. Sci. USA 92:6097-101; non-ionic backbones (U.S. Patent Nos. 5,386,023, 5,637,684, 5,602,240, 5,216,141 and 4,469,863; Kiedrowshi, et al. (1991) Angew. Chem. Intl. Ed. English 30:423-426; Letsinger, et al. (1988) J. Am. Chem. Soc. 110:4470;

Letsinger, et al. (1994) Nucleoside and Nucleotide 13:1597-xxx; Chapters 2 and 3 in Sanghvi and Cook (eds. 1994) Carbohydrate Modifications in Antisense Research ACS Symposium Series 580; Mesmaeker, et al. (1994) Bioorganic and Medicinal Chem. Lett. 4:395-xxx; Jeffs, et al. (1994) J. Biomolecular NMR 34:17; Horn (1996) Tetrahedron Lett. 37:743-xxx) and non-ribose backbones, including those described in U.S. Patent Nos. 5,235,033 and 5,034,506, and Chapters 6 and 7 in Sanghvi and Cook (eds. 1994) Carbohydrate Modifications in Antisense Research ACS Symposium Series 580. Nucleic acids containing one or more carbocyclic sugars are also included within one definition of nucleic acids (see Jenkins, et al. (1995) Chem. Soc. Rev. xx:169-176). Several nucleic acid analogs are described in Rawls (p. 35, June 2, 1997) C&E News. Each of these references is hereby expressly incorporated by reference.

Particularly preferred are peptide nucleic acids (PNA) which includes peptide nucleic acid analogs. These backbones are substantially non-ionic under neutral conditions, in contrast to the highly charged phosphodiester backbone of naturally occurring nucleic acids. This results in two advantages. First, the PNA backbone exhibits improved hybridization kinetics. PNAs have larger changes in the melting temperature (T_m) for mismatched versus perfectly matched base pairs. DNA and RNA typically exhibit a 2-4° C drop in T_m for an internal mismatch. With the non-ionic PNA backbone, the drop is closer to 7-9° C. Similarly, due to their non-ionic nature, hybridization of the bases attached to these backbones is relatively insensitive to salt concentration. In addition, PNAs are not degraded by cellular enzymes, and thus can be more stable.

The nucleic acids may be single stranded or double stranded, as specified, or contain portions of both double stranded or single stranded sequence. As will be appreciated by those in the art, the depiction of a single strand also defines the sequence of the complementary strand; thus the sequences described herein also provide the complement of the sequence. The nucleic acid may be DNA, both genomic and cDNA, RNA or a hybrid, where the nucleic acid may contain combinations of deoxyribo- and ribo-nucleotides, and combinations of bases, including uracil, adenine, thymine, cytosine, guanine, inosine, xanthine hypoxanthine, isocytosine, isoguanine, etc. "Transcript" typically refers to a naturally occurring RNA, e.g., a pre-mRNA, hnRNA, or mRNA. As used herein, the term "nucleoside" includes nucleotides and nucleoside and nucleotide analogs, and modified nucleosides such as amino modified nucleosides. In addition, "nucleoside" includes non-naturally occurring analog structures.

Thus, e.g., the individual units of a peptide nucleic acid, each containing a base, are referred to herein as a nucleoside.

A "label" or a "detectable moiety" is a composition detectable by spectroscopic, photochemical, biochemical, immunochemical, chemical, or other physical means. For example, useful labels include ^{32}P , fluorescent dyes, electron-dense reagents, enzymes (e.g., as commonly used in an ELISA), biotin, digoxigenin, or haptens and proteins or other entities which can be made detectable, e.g., by incorporating a radiolabel into the peptide or used to detect antibodies specifically reactive with the peptide. The labels may be incorporated into the prostate cancer nucleic acids, proteins, and antibodies at virtually any position. Many methods for conjugating the antibody to the label may be employed, including those methods described by Hunter, et al. (1962) Nature, 144:945; David, et al. (1974) Biochemistry 13:1014-1021; Pain, et al. (1981) J. Immunol. Meth. 40:219-230; and Nygren (1982) J. Histochem. and Cytochem. 30:407-412.

An "effector" or "effector moiety" or "effector component" is a molecule that is bound (or linked, or conjugated), either covalently, through a linker or a chemical bond, or noncovalently, through ionic, van der Waals, electrostatic, or hydrogen bonds, to an antibody. The "effector" can be a variety of molecules including, e.g., detection moieties including radioactive compounds, fluorescent compounds, an enzyme or substrate, tags such as epitope tags, a toxin; activatable moieties, a chemotherapeutic agent; a lipase; an antibiotic; or a radioisotope emitting "hard" e.g., beta radiation.

A "labeled nucleic acid probe or oligonucleotide" is one that is bound, either covalently, through a linker or a chemical bond, or noncovalently, through ionic, van der Waals, electrostatic, or hydrogen bonds to a label such that the presence of the probe may be detected by detecting the presence of the label bound to the probe. Alternatively, method using high affinity interactions may achieve the same results where one of a pair of binding partners binds to the other, e.g., biotin, streptavidin.

As used herein a "nucleic acid probe or oligonucleotide" is defined as a nucleic acid capable of binding to a target nucleic acid of complementary sequence through one or more types of chemical bonds, usually through complementary base pairing, usually through hydrogen bond formation. As used herein, a probe may include natural (i.e., A, G, C, or T) or modified bases (7-deazaguanosine, inosine, etc.). In addition, the bases in a probe may be joined by a linkage other than a phosphodiester bond, so long as it does not functionally

interfere with hybridization. Thus, e.g., probes may be peptide nucleic acids in which the constituent bases are joined by peptide bonds rather than phosphodiester linkages. It will be understood by one of skill in the art that probes may bind target sequences lacking complete complementarity with the probe sequence depending upon the stringency of the hybridization conditions. The probes are preferably directly labeled as with isotopes, chromophores, lumiphores, chromogens, or indirectly labeled such as with biotin to which a streptavidin complex may later bind. By assaying for the presence or absence of the probe, one can detect the presence or absence of the select sequence or subsequence. Diagnosis or prognosis may be based at the genomic level, or at the level of RNA or protein expression.

The term "recombinant" when used with reference, e.g., to a cell, or nucleic acid, protein, or vector, indicates that the cell, nucleic acid, protein or vector, has been modified by the introduction of a heterologous nucleic acid or protein or the alteration of a native nucleic acid or protein, or that the cell is derived from a cell so modified. Thus, e.g., recombinant cells express genes that are not found within the native (non-recombinant) form of the cell or express native genes that are otherwise abnormally expressed, under expressed or not expressed at all. By the term "recombinant nucleic acid" herein is meant nucleic acid, originally formed in vitro, in general, by the manipulation of nucleic acid, e.g., using polymerases and endonucleases, in a form not normally found in nature. In this manner, operably linkage of different sequences is achieved. Thus an isolated nucleic acid, in a linear form, or an expression vector formed in vitro by ligating DNA molecules that are not normally joined, are both considered recombinant for the purposes of this invention. It is understood that once a recombinant nucleic acid is made and reintroduced into a host cell or organism, it will replicate non-recombinantly, i.e., using the in vivo cellular machinery of the host cell rather than in vitro manipulations; however, such nucleic acids, once produced recombinantly, although subsequently replicated non-recombinantly, are still considered recombinant for the purposes of the invention. Similarly, a "recombinant protein" is a protein made using recombinant techniques, i.e., through the expression of a recombinant nucleic acid as depicted above.

The term "heterologous" when used with reference to portions of a nucleic acid indicates that the nucleic acid comprises two or more subsequences that are not normally found in the same relationship to each other in nature. For instance, the nucleic acid is typically recombinantly produced, having two or more sequences, e.g., from unrelated genes

arranged to make a new functional nucleic acid, e.g., a promoter from one source and a coding region from another source. Similarly, a heterologous protein will often refer to two or more subsequences that are not found in the same relationship to each other in nature (e.g., a fusion protein).

5 A “promoter” is defined as an array of nucleic acid control sequences that direct transcription of a nucleic acid. As used herein, a promoter includes necessary nucleic acid sequences near the start site of transcription, such as, in the case of a polymerase II type promoter, a TATA element. A promoter also optionally includes distal enhancer or repressor elements, which can be located as much as several thousand base pairs from the start site of
10 transcription. A “constitutive” promoter is a promoter that is active under most environmental and developmental conditions. An “inducible” promoter is a promoter that is active under environmental or developmental regulation. The term “operably linked” refers to a functional linkage between a nucleic acid expression control sequence (such as a promoter, or array of transcription factor binding sites) and a second nucleic acid sequence,
15 wherein the expression control sequence directs transcription of the nucleic acid corresponding to the second sequence.

An “expression vector” is a nucleic acid construct, generated recombinantly or synthetically, with a series of specified nucleic acid elements that permit transcription of a particular nucleic acid in a host cell. The expression vector can be part of a plasmid, virus, or
20 nucleic acid fragment. Typically, the expression vector includes a nucleic acid to be transcribed operably linked to a promoter.

The phrase “selectively (or specifically) hybridizes to” refers to the binding, duplexing, or hybridizing of a molecule only to a particular nucleotide sequence under stringent hybridization conditions when that sequence is present in a complex mixture (e.g.,
25 total cellular or library DNA or RNA).

The phrase “stringent hybridization conditions” refers to conditions under which a probe will hybridize to its target subsequence, typically in a complex mixture of nucleic acids, but to no other sequences. Stringent conditions are sequence-dependent and will be different in different circumstances. Longer sequences hybridize specifically at higher
30 temperatures. An extensive guide to the hybridization of nucleic acids is found “Overview of principles of hybridization and the strategy of nucleic acid assays” in Tijssen (1993) Hybridization with Nucleic Probes (Techniques in Biochemistry and Molecular Biology vol.

24) Elsevier. Generally, stringent conditions are selected to be about 5-10° C lower than the thermal melting point (T_m) for the specific sequence at a defined ionic strength pH. The T_m is the temperature (under defined ionic strength, pH, and nucleic concentration) at which 50% of the probes complementary to the target hybridize to the target sequence at equilibrium (as the target sequences are present in excess, at T_m , 50% of the probes are occupied at equilibrium). Stringent conditions will be those in which the salt concentration is less than about 1.0 M sodium ion, typically about 0.01 to 1.0 M sodium ion concentration (or other salts) at pH 7.0 to 8.3 and the temperature is at least about 30° C for short probes (e.g., 10 to 50 nucleotides) and at least about 60° C for long probes (e.g., greater than 50 nucleotides).

Stringent conditions may also be achieved with the addition of destabilizing agents such as formamide. For selective or specific hybridization, a positive signal is at least two times background, preferably 10 times background hybridization. Exemplary stringent hybridization conditions can be as following: 50% formamide, 5x SSC, and 1% SDS, incubating at 42° C, or, 5x SSC, 1% SDS, incubating at 65° C, with wash in 0.2x SSC, and 0.1% SDS at 65° C. For PCR, a temperature of about 36° C is typical for low stringency amplification, although annealing temperatures may vary between about 32° C and 48° C depending on primer length. For high stringency PCR amplification, a temperature of about 62° C is typical, although high stringency annealing temperatures can range from about 50-65° C, depending on the primer length and specificity. Typical cycle conditions for both high and low stringency amplifications include a denaturation phase of 90-95° C for 30-120 sec, an annealing phase lasting 30-120 sec, and an extension phase of about 72° C for 1-2 min. Protocols and guidelines for low and high stringency amplification reactions are provided, e.g., in Innis, et al. (1990) PCR Protocols: A Guide to Methods and Applications Academic Press, N.Y.

Nucleic acids that do not hybridize to each other under stringent conditions are still substantially identical if the polypeptides which they encode are substantially identical. This occurs, e.g., when a copy of a nucleic acid is created using the maximum codon degeneracy permitted by the genetic code. In such cases, the nucleic acids typically hybridize under moderately stringent hybridization conditions. Exemplary "moderately stringent hybridization conditions" include a hybridization in a buffer of 40% formamide, 1 M NaCl, 1% SDS at 37° C, and a wash in 1X SSC at 45° C. A positive hybridization is at least twice

background. Those of ordinary skill will readily recognize that alternative hybridization and wash conditions can be utilized to provide conditions of similar stringency. Additional guidelines for determining hybridization parameters are provided in numerous references, e.g., Ausubel, et al. (eds. 1991 and supplements) Current Protocols in Molecular Biology

5 The phrase “functional effects” in the context of assays for testing compounds that modulate activity of a prostate cancer protein includes the determination of a parameter that is indirectly or directly under the influence of the prostate cancer protein or nucleic acid, e.g., a functional, physical, or chemical effect, such as the ability to decrease prostate proliferation (malignant or non-malignant). It includes ligand binding activity; cell growth on soft agar;
10 anchorage dependence; contact inhibition and density limitation of growth; cellular proliferation; cellular transformation; growth factor or serum dependence; tumor specific marker levels; invasiveness into Matrigel; tumor growth and metastasis in vivo; mRNA and protein expression in cells undergoing metastasis, and other characteristics of prostate cancer cells. “Functional effects” include in vitro, in vivo, and ex vivo activities.

15 By “determining the functional effect” is meant assaying for a compound that increases or decreases a parameter that is indirectly or directly under the influence of a prostate cancer protein sequence, e.g., functional, enzymatic, physical and chemical effects. Such functional effects can be measured by means known to those skilled in the art, e.g., changes in spectroscopic characteristics (e.g., fluorescence, absorbance, refractive index),
20 hydrodynamic (e.g., shape), chromatographic, or solubility properties for the protein, measuring inducible markers or transcriptional activation of the prostate cancer protein; measuring binding activity or binding assays, e.g., binding to antibodies or other ligands, and measuring cellular proliferation. Determination of the functional effect of a compound on prostate cancer can also be performed using prostate cancer assays known to those of skill in
25 the art such as an in vitro assays, e.g., cell growth on soft agar; anchorage dependence; contact inhibition and density limitation of growth; cellular proliferation; cellular transformation; growth factor or serum dependence; tumor specific marker levels; invasiveness into Matrigel; tumor growth and metastasis in vivo; mRNA and protein expression in cells undergoing metastasis, and other characteristics of prostate cancer cells.
30 The functional effects can be evaluated by many means known to those skilled in the art, e.g., microscopy for quantitative or qualitative measures of alterations in morphological features, measurement of changes in RNA or protein levels for prostate cancer-associated sequences,

measurement of RNA stability, identification of downstream or reporter gene expression (CAT, luciferase, β -gal, GFP, and the like), e.g., via chemiluminescence, fluorescence, colorimetric reactions, antibody binding, inducible markers, and ligand binding assays.

“Inhibitors”, “activators”, and “modulators” of prostate cancer polynucleotide and polypeptide sequences are used to refer to activating, inhibitory, or modulating molecules or compounds identified using in vitro and in vivo assays of prostate cancer polynucleotide and polypeptide sequences. Inhibitors are compounds that, e.g., bind to, partially or totally block activity, decrease, prevent, delay activation, inactivate, desensitize, or down regulate the activity or expression of prostate cancer proteins, e.g., antagonists. Antisense nucleic acids may seem to inhibit expression and subsequent function of the protein. “Activators” are compounds that increase, open, activate, facilitate, enhance activation, sensitize, agonize, or up regulate prostate cancer protein activity. Inhibitors, activators, or modulators also include genetically modified versions of prostate cancer proteins, e.g., versions with altered activity, as well as naturally occurring and synthetic ligands, antagonists, agonists, antibodies, small chemical molecules and the like. Such assays for inhibitors and activators include, e.g., expressing the prostate cancer protein in vitro, in cells, or cell membranes, applying putative modulator compounds, and then determining the functional effects on activity, as described above. Activators and inhibitors of prostate cancer can also be identified by incubating prostate cancer cells with the test compound and determining increases or decreases in the expression of 1 or more prostate cancer proteins, e.g., 1, 2, 3, 4, 5, 10, 15, 20, 25, 30, 40, 50 or more prostate cancer proteins, such as prostate cancer proteins encoded by the sequences set out in Tables 1A-4.

Samples or assays comprising prostate cancer proteins that are treated with a potential activator, inhibitor, or modulator are compared to control samples without the inhibitor, activator, or modulator to examine the extent of inhibition. Control samples (untreated with inhibitors) are assigned a relative protein activity value of 100%. Inhibition of a polypeptide is achieved when the activity value relative to the control is about 80%, preferably 50%, more preferably 25-0%. Activation of a prostate cancer polypeptide is achieved when the activity value relative to the control (untreated with activators) is 110%, more preferably 150%, more preferably 200-500% (i.e., two to five fold higher relative to the control), more preferably 1000-3000% higher.

The phrase “changes in cell growth” refers to a change in cell growth and proliferation characteristics in vitro or in vivo, such as cell viability, formation of foci, anchorage independence, semi-solid or soft agar growth, changes in contact inhibition and density limitation of growth, loss of growth factor or serum requirements, changes in cell morphology, gaining or losing immortalization, gaining or losing tumor specific markers, ability to form or suppress tumors when injected into suitable animal hosts, and/or immortalization of the cell. See, e.g., pp. 231-241 in Freshney (1994) Culture of Animal Cells: A Manual of Basic Technique (3d ed.) Wiley-Liss.

“Tumor cell” refers to precancerous, cancerous, and/or normal cells in a tumor.

“Cancer cells,” “transformed” cells, or “transformation” in tissue culture, refers to spontaneous or induced phenotypic changes that do not necessarily involve the uptake of new genetic material. Although transformation can arise from infection with a transforming virus and incorporation of new genomic DNA, or uptake of exogenous DNA, it can also arise spontaneously or following exposure to a carcinogen, thereby mutating an endogenous gene. Transformation is associated with phenotypic changes, such as immortalization of cells, aberrant growth control, nonmorphological changes, and/or malignancy. See, Freshney (2001) Culture of Animal Cells: A Manual of Basic Technique (4th ed.) Wiley-Liss.

“Antibody” refers to a polypeptide comprising a framework region from an immunoglobulin gene or fragments thereof that specifically binds and recognizes an antigen.

The recognized immunoglobulin genes include the kappa, lambda, alpha, gamma, delta, epsilon, and mu constant region genes, as well as the myriad immunoglobulin variable region genes. Light chains are classified as either kappa or lambda. Heavy chains are classified as gamma, mu, alpha, delta, or epsilon, which in turn define the immunoglobulin classes, IgG, IgM, IgA, IgD, and IgE, respectively. Typically, the antigen-binding region of an antibody or its functional equivalent will be most critical in specificity and affinity of binding. See Paul (ed. 1999) Fundamental Immunology (4th ed.) Raven.

An exemplary immunoglobulin (antibody) structural unit comprises a tetramer. Each tetramer is composed of two identical pairs of polypeptide chains, each pair having one “light” (about 25 kD) and one “heavy” chain (about 50-70 kD). The N-terminus of each chain defines a variable region of about 100 to 110 or more amino acids primarily responsible for antigen recognition. The terms variable light chain (V_L) and variable heavy chain (V_H) refer to these light and heavy chains respectively.

Antibodies exist, e.g., as intact immunoglobulins or as a number of well-characterized fragments produced by digestion with various peptidases. Thus, e.g., pepsin digests an antibody below the disulfide linkages in the hinge region to produce $F(ab)'_2$, a dimer of Fab which itself is a light chain joined to V_H - C_H1 by a disulfide bond. The $F(ab)'_2$ may be
5 reduced under mild conditions to break the disulfide linkage in the hinge region, thereby converting the $F(ab)'_2$ dimer into an Fab' monomer. The Fab' monomer is essentially Fab with part of the hinge region (see Paul (ed. 1993) Fundamental Immunology (3d ed.) Raven. While various antibody fragments are defined in terms of the digestion of an intact antibody, one of skill will appreciate that such fragments may be synthesized de novo either chemically
10 or by using recombinant DNA methodology. Thus, the term antibody, as used herein, also includes antibody fragments either produced by the modification of whole antibodies, or those synthesized de novo using recombinant DNA methodologies (e.g., single chain Fv) or those identified using phage display libraries (see, e.g., McCafferty, et al.(1990) Nature 348:552-554.

15 For preparation of antibodies, e.g., recombinant, monoclonal, or polyclonal antibodies, many technique known in the art can be used (see, e.g., Kohler and Milstein (1975) Nature 256:495-497; Kozbor, et al. (1983) Immunology Today 4:72; pp. 77-96 in Cole, et al. (1985) Monoclonal Antibodies and Cancer Therapy Liss; Coligan (1991) Current Protocols in Immunology Lippincott; Harlow and Lane (1988) Antibodies: A Laboratory
20 Manual CSH Press; and Goding (1986) Monoclonal Antibodies: Principles and Practice (2d ed.) Academic Press. Techniques for the production of single chain antibodies (U.S. Patent 4,946,778) can be adapted to produce antibodies to polypeptides of this invention. Also, transgenic mice, or other organisms such as other mammals, may be used to express humanized antibodies. Alternatively, phage display technology can be used to identify
25 antibodies and heteromeric Fab fragments that specifically bind to selected antigens (see, e.g., McCafferty, et al. (1990) Nature 348:552-554; Marks, et al. (1992) Biotechnology 10:779-783).

A "chimeric antibody" is an antibody molecule in which (a) the constant region, or a portion thereof, is altered, replaced or exchanged so that the antigen binding site (variable
30 region) is linked to a constant region of a different or altered class, effector function and/or species, or an entirely different molecule which confers new properties to the chimeric antibody, e.g., an enzyme, toxin, hormone, growth factor, drug, etc.; or (b) the variable

region, or a portion thereof, is altered, replaced or exchanged with a variable region having a different or altered antigen specificity.

Identification of prostate cancer-associated sequences

- 5 In one aspect, the expression levels of genes are determined in different patient samples for which diagnosis information is desired, to provide expression profiles. An expression profile of a particular sample is essentially a “fingerprint” of the state of the sample; while two states may have a particular gene similarly expressed, the evaluation of a number of genes simultaneously allows the generation of a gene expression profile that is
- 10 characteristic of the state of the cell. That is, normal tissue (e.g., normal prostate or other tissue) may be distinguished from pathological prostate cells, e.g., cancerous or metastatic cancerous tissue of the prostate, or prostate cancer tissue or metastatic prostate cancerous tissue can be compared with tissue samples of prostate and other tissues from surviving cancer patients. By comparing expression profiles of tissue in known different prostate
- 15 cancer states, information regarding which genes are important (including both up- and down-regulation of genes) in each of these states is obtained.

- The identification of sequences that are differentially expressed in prostate cancer versus non-prostate cancer tissue allows the use of this information in a number of ways. For example, a particular treatment regime may be evaluated: does a chemotherapeutic drug act
- 20 to down-regulate prostate cancer or other proliferative disorders, and thus tumor growth or recurrence, in a particular patient. Alternatively, a treatment step may induce other markers which may be used as targets to destroy tumor cells. Similarly, diagnosis and treatment outcomes may be done or confirmed by comparing patient samples with the known expression profiles. Malignant disease may be compared to non-malignant conditions.
- 25 Metastatic tissue can also be analyzed to determine the stage of prostate cancer in the tissue, or origin of primary tumor, e.g., metastasis from a remote primary site. Furthermore, these gene expression profiles (or individual genes) allow screening of drug candidates with an eye to mimicking or altering a particular expression profile; e.g., screening can be done for drugs that suppress the prostate cancer expression profile. This may be done by making biochips
- 30 comprising sets of the important prostate cancer genes, which can then be used in these screens. These methods can also be done on the protein basis; that is, protein expression levels of the prostate cancer proteins can be evaluated for diagnostic purposes or to screen

candidate agents. In addition, the prostate cancer nucleic acid sequences can be administered for gene therapy purposes, including the administration of antisense nucleic acids, or the prostate cancer proteins (including antibodies and other modulators thereof) administered as therapeutic drugs.

5 Thus the present invention provides nucleic acid and protein sequences that are differentially expressed in prostate cancer relative to normal tissues and/or non-malignant disease, or in different types of related diseases, herein termed "prostate cancer sequences." As outlined below, prostate cancer sequences include those that are up-regulated (i.e., expressed at a higher level) in prostate cancer, as well as those that are down-regulated (i.e.,
10 expressed at a lower level). In a preferred embodiment, the prostate cancer sequences are from humans; however, as will be appreciated by those in the art, prostate cancer sequences from other organisms may be useful in animal models of disease and drug evaluation; thus, other prostate cancer sequences are provided, from vertebrates, including mammals, including rodents (rats, mice, hamsters, guinea pigs, etc.), primates, farm animals (including
15 sheep, goats, pigs, cows, horses, etc.) and pets, e.g., (dogs, cats, etc.). Prostate cancer sequences from other organisms may be obtained using the techniques outlined below.

Prostate cancer sequences can include both nucleic acid and amino acid sequences. As will be appreciated by those in the art and is more fully outlined below, prostate cancer nucleic acid sequences are useful in a variety of applications, including diagnostic
20 applications, which will detect naturally occurring nucleic acids, as well as screening applications; e.g., biochips comprising nucleic acid probes or PCR microtiter plates with selected probes to the prostate cancer sequences can be generated.

A prostate cancer sequence can be initially identified by substantial nucleic acid and/or amino acid sequence homology to the prostate cancer sequences outlined herein. Such
25 homology can be based upon the overall nucleic acid or amino acid sequence, and is generally determined as outlined below, using either homology programs or hybridization conditions.

For identifying prostate cancer-associated sequences, the prostate cancer screen typically includes comparing genes identified in different tissues, e.g., normal and cancerous
30 tissues, or tumor tissue samples from patients who have metastatic disease vs. non metastatic tissue. Other suitable tissue comparisons include comparing prostate cancer samples with metastatic cancer samples from other cancers, such as lung, breast, gastrointestinal cancers,

ovarian, etc. Samples of different stages of prostate cancer, e.g., survivor tissue, drug resistant states, and tissue undergoing metastasis, are applied to biochips comprising nucleic acid probes. The samples are first microdissected, if applicable, and treated as is known in the art for the preparation of mRNA. Suitable biochips are commercially available, e.g., from
5 Affymetrix. Gene expression profiles are generated and the data analyzed.

In one embodiment, the genes showing changes in expression as between normal and disease states are compared to genes expressed in other normal tissues, preferably normal prostate, but also including, and not limited to lung, heart, brain, liver, breast, kidney, muscle, colon, small intestine, large intestine, spleen, bone, and placenta. In a preferred embodiment,
10 those genes identified during the prostate cancer screen that are expressed in a significant amount in other tissues are removed from the profile, although in some embodiments, this is not necessary. That is, when screening for drugs, it is usually preferable that the target be disease specific, to minimize possible side effects on other organs were there expression.

In a preferred embodiment, prostate cancer sequences are those that are up-regulated in prostate cancer or related conditions; that is, the expression of these genes is higher in the
15 prostate cancer tissue as compared to non-cancerous tissue. "Up-regulation" as used herein often means at least about a two-fold change, preferably at least about a three fold change, with at least about five-fold or higher being preferred. Another embodiment is directed to sequences up-regulated in non-malignant conditions relative to normal.

Unigene cluster identification numbers and accession numbers herein are for the
20 GenBank sequence database and the sequences of the accession numbers are hereby expressly incorporated by reference. GenBank is known in the art, see, e.g., Benson, et al. (1998) Nucleic Acids Research 26:1-7 and <http://www.ncbi.nlm.nih.gov/>. Sequences are also available in other databases, e.g., European Molecular Biology Laboratory (EMBL) and
25 DNA Database of Japan (DDBJ). U.S. Patent Application N. 09/687,576 and 09/976,858 (-001-3) further disclose related sequences, compositions, and methods of diagnosis and treatment of prostate cancer and related conditions and are hereby expressly incorporated by reference.

In another preferred embodiment, prostate cancer sequences are those that are down-regulated in the prostate cancer; that is, the expression of these genes is lower in prostate
30 cancer tissue as compared to non-cancerous tissue. "Down-regulation" as used herein often

means at least about a two-fold change, preferably at least about a three fold change, with at least about five-fold or higher being preferred.

Informatics

5 The ability to identify genes that are over or under expressed in prostate cancer can additionally provide high-resolution, high-sensitivity datasets which can be used in the areas of diagnostics, therapeutics, drug development, pharmacogenetics, protein structure, biosensor development, and other related areas. For example, the expression profiles can be used in diagnostic or prognostic evaluation of patients with prostate cancer. Or as another
10 example, subcellular toxicological information can be generated to better direct drug structure and activity correlation (see Anderson, Pharmaceutical Proteomics: Targets, Mechanism, and Function, paper presented at the IBC Proteomics conference, Coronado, CA (June 11-12, 1998)). Subcellular toxicological information can also be utilized in a biological sensor device to predict the likely toxicological effect of chemical exposures and likely tolerable
15 exposure thresholds (see U.S. Patent No. 5,811,231). Similar advantages accrue from datasets relevant to other biomolecules and bioactive agents (e.g., nucleic acids, saccharides, lipids, drugs, and the like).

 Thus, in another embodiment, the present invention provides a database that includes at least one set of assay data. The data contained in the database is acquired, e.g., using array
20 analysis either singly or in a library format. The database can be in a form in which data can be maintained and transmitted, but is preferably an electronic database. The electronic database of the invention can be maintained on an electronic device allowing for the storage of and access to the database, such as a personal computer, but is preferably distributed on a wide area network, such as the World Wide Web.

25 The focus of the present section on databases that include peptide sequence data is for clarity of illustration only. It will be apparent to those of skill in the art that similar databases can be assembled for assay data acquired using an assay of the invention.

 The compositions and methods for identifying and/or quantitating the relative and/or absolute abundance of a variety of molecular and macromolecular species from a biological
30 sample undergoing prostate cancer, i.e., the identification of prostate cancer-associated sequences described herein, provide an abundance of information, which can be correlated with pathological conditions, predisposition to disease, drug testing, therapeutic monitoring,

gene-disease causal linkages, identification of correlates of immunity and physiological status, among others. Although the data generated from the assays of the invention is suited for manual review and analysis, in a preferred embodiment, prior data processing using high-speed computers is utilized.

5 An array of methods for indexing and retrieving biomolecular information is known in the art. For example, U.S. Patents 6,023,659 and 5,966,712 disclose a relational database system for storing biomolecular sequence information in a manner that allows sequences to be catalogued and searched according to one or more protein function hierarchies. U.S. Patent 5,953,727 discloses a relational database having sequence records containing
10 information in a format that allows a collection of partial-length DNA sequences to be catalogued and searched according to association with one or more sequencing projects for obtaining full-length sequences from the collection of partial length sequences. U.S. Patent 5,706,498 discloses a gene database retrieval system for making a retrieval of a gene sequence similar to a sequence data item in a gene database based on the degree of similarity
15 between a key sequence and a target sequence. U.S. Patent 5,538,897 discloses a method using mass spectroscopy fragmentation patterns of peptides to identify amino acid sequences in computer databases by comparison of predicted mass spectra with experimentally-derived mass spectra using a closeness-of-fit measure. U.S. Patent 5,926,818 discloses a multi-dimensional database comprising a functionality for multi-dimensional data analysis
20 described as on-line analytical processing (OLAP), which entails the consolidation of projected and actual data according to more than one consolidation path or dimension. U.S. Patent 5,295,261 reports a hybrid database structure in which the fields of each database record are divided into two classes, navigational and informational data, with navigational fields stored in a hierarchical topological map which can be viewed as a tree structure or as
25 the merger of two or more such tree structures.

See also Mount, et al. (2001) Bioinformatics CSH Press; Durbin, et al. (eds. 1999) Biological Sequence Analysis: Probabilistic Models of Proteins and Nucleic Acids Cambridge Univ. Press; Baxevanis and Ouellette (eds., 1998) Bioinformatics: A Practical Guide to the Analysis of Genes and Proteins Wiley-Liss; Rashidi and Buehler (1999) Bioinformatics: Basic Applications in Biological Science and Medicine CRC Press; Setubal, et al. (eds. 1997) Introduction to Computational Molecular Biology Brooks/Cole; Misener and Krawetz (eds. 2000) Bioinformatics: Methods and Protocols Human Press; Higgins and
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- Taylor (eds. 2000) Bioinformatics: Sequence, Structure, and Databanks: A Practical Approach Oxford Univ. Press; Brown (2001) Bioinformatics: A Biologist's Guide to Biocomputing and the Internet Eaton Pub; Han and Kamber (2000) Data Mining: Concepts and Techniques Kaufmann Pub.; and Waterman (1995) Introduction to Computational Biology: Maps, Sequences, and Genomes Chap and Hall.

The present invention provides a computer database comprising a computer and software for storing in computer-retrievable form assay data records cross-tabulated, e.g., with data specifying the source of the target-containing sample from which each sequence specificity record was obtained.

- In an exemplary embodiment, at least one of the sources of target-containing sample is from a control tissue sample known to be free of pathological disorders. In a variation, at least one of the sources is a known pathological tissue specimen, e.g., a neoplastic lesion or another tissue specimen to be analyzed for prostate cancer. In another variation, the assay records cross-tabulate one or more of the following parameters for each target species in a sample: (1) a unique identification code, which can include, e.g., a target molecular structure and/or characteristic separation coordinate (e.g., electrophoretic coordinates); (2) sample source; and (3) absolute and/or relative quantity of the target species present in the sample.

- The invention also provides for the storage and retrieval of a collection of target data in a computer data storage apparatus, which can include magnetic disks, optical disks, magneto-optical disks, DRAM, SRAM, SGRAM, SDRAM, RDRAM, DDR RAM, magnetic bubble memory devices, and other data storage devices, including CPU registers and on-CPU data storage arrays. Typically, the target data records are stored as a bit pattern in an array of magnetic domains on a magnetizable medium or as an array of charge states or transistor gate states, such as an array of cells in a DRAM device (e.g., each cell comprised of a transistor and a charge storage area, which may be on the transistor). In one embodiment, the invention provides such storage devices, and computer systems built therewith, comprising a bit pattern encoding a protein expression fingerprint record comprising unique identifiers for at least 10 target data records cross-tabulated with target source.

- When the target is a peptide or nucleic acid, the invention preferably provides a method for identifying related peptide or nucleic acid sequences, comprising performing a computerized comparison between a peptide or nucleic acid sequence assay record stored in or retrieved from a computer storage device or database and at least one other sequence. The

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comparison can include a sequence analysis or comparison algorithm or computer program embodiment thereof (e.g., FASTA, TFASTA, GAP, BESTFIT) and/or the comparison may be of the relative amount of a peptide or nucleic acid sequence in a pool of sequences determined from a polypeptide or nucleic acid sample of a specimen.

5 The invention also preferably provides a magnetic disk, such as an IBM-compatible (DOS, Windows, Windows95/98/2000, Windows NT, OS/2) or other format (e.g., Linux, SunOS, Solaris, AIX, SCO Unix, VMS, MV, Macintosh, etc.) floppy diskette or hard (fixed, Winchester) disk drive, comprising a bit pattern encoding data from an assay of the invention in a file format suitable for retrieval and processing in a computerized sequence analysis,
10 comparison, or relative quantitation method.

 The invention also provides a network, comprising a plurality of computing devices linked via a data link, such as an Ethernet cable (coax or 10BaseT), telephone line, ISDN line, wireless network, optical fiber, or other suitable signal transmission medium, whereby at least one network device (e.g., computer, disk array, etc.) comprises a pattern of magnetic
15 domains (e.g., magnetic disk) and/or charge domains (e.g., an array of DRAM cells) composing a bit pattern encoding data acquired from an assay of the invention.

 The invention also provides a method for transmitting assay data that includes generating an electronic signal on an electronic communications device, such as a modem, ISDN terminal adapter, DSL, cable modem, ATM switch, or the like, wherein the signal
20 includes (in native or encrypted format) a bit pattern encoding data from an assay or a database comprising a plurality of assay results obtained by the method of the invention.

 In a preferred embodiment, the invention provides a computer system for comparing a query target to a database containing an array of data structures, such as an assay result obtained by the method of the invention, and ranking database targets based on the degree of
25 identity and gap weight to the target data. A central processor is preferably initialized to load and execute the computer program for alignment and/or comparison of the assay results. Data for a query target is entered into the central processor via an I/O device. Execution of the computer program results in the central processor retrieving the assay data from the data file, which comprises a binary description of an assay result.

30 The target data or record and the computer program can be transferred to secondary memory, which is typically random access memory (e.g., DRAM, SRAM, SGRAM, or SDRAM). Targets are ranked according to the degree of correspondence between a selected

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assay characteristic (e.g., binding to a selected affinity moiety) and the same characteristic of the query target and results are output via an I/O device. For example, a central processor can be a conventional computer (e.g., Intel Pentium, PowerPC, Alpha, PA-8000, SPARC, MIPS 4400, MIPS 10000, VAX, etc.); a program can be a commercial or public domain
5 molecular biology software package (e.g., UWGCG Sequence Analysis Software, Darwin); a data file can be an optical or magnetic disk, a data server, a memory device (e.g., DRAM, SRAM, SGRAM, SDRAM, EPROM, bubble memory, flash memory, etc.); an I/O device can be a terminal comprising a video display and a keyboard, a modem, an ISDN terminal adapter, an Ethernet port, a punched card reader, a magnetic strip reader, or other suitable I/O
10 device.

The invention also preferably provides the use of a computer system, such as that described above, which comprises: (1) a computer; (2) a stored bit pattern encoding a collection of peptide sequence specificity records obtained by the methods of the invention, which may be stored in the computer; (3) a comparison target, such as a query target; and (4)
15 a program for alignment and comparison, typically with rank-ordering of comparison results on the basis of computed similarity values.

Characteristics of prostate cancer-associated proteins

Prostate cancer proteins of the present invention may be classified as secreted
20 proteins, transmembrane proteins, or intracellular proteins. In one embodiment, the prostate cancer protein is an intracellular protein. Intracellular proteins may be found in the cytoplasm and/or in the nucleus. Intracellular proteins are involved in all aspects of cellular function and replication (including, e.g., signaling pathways); aberrant expression of such proteins often results in unregulated or dysregulated cellular processes (see, e.g., Alberts (ed.
25 1994) Molecular Biology of the Cell (3d ed.) Garland. For example, many intracellular proteins have enzymatic activity such as protein kinase activity, protein phosphatase activity, protease activity, nucleotide cyclase activity, polymerase activity and the like. Intracellular proteins also serve as docking proteins that are involved in organizing complexes of proteins, or targeting proteins to various subcellular localizations, and are involved in maintaining the
30 structural integrity of organelles.

An increasingly appreciated concept in characterizing proteins is the presence in the proteins of one or more structural motifs for which defined functions have been attributed. In

addition to the highly conserved sequences found in the enzymatic domain of proteins, highly conserved sequences have been identified in proteins that are involved in protein-protein interaction. For example, Src-homology-2 (SH2) domains bind tyrosine-phosphorylated targets in a sequence dependent manner. PTB domains, which are distinct from SH2 domains, also bind tyrosine phosphorylated targets. SH3 domains bind to proline-rich targets. In addition, PH domains, tetratricopeptide repeats and WD domains to name only a few, have been shown to mediate protein-protein interactions. Some of these may also be involved in binding to phospholipids or other second messengers. As will be appreciated by one of ordinary skill in the art, these motifs can be identified on the basis of amino acid sequence; thus, an analysis of the sequence of proteins may provide insight into both the enzymatic potential of the molecule and/or molecules with which the protein may associate. One useful database is Pfam (protein families), which is a large collection of multiple sequence alignments and hidden Markov models covering many common protein domains. Versions are available via the internet from Washington University in St. Louis, the Sanger Center in England, and the Karolinska Institute in Sweden (see, e.g., Bateman, et al. (2000) Nuc. Acids Res. 28:263-266; Sonnhammer, et al. (1997) Proteins 28:405-420; Bateman, et al. (1999) Nuc. Acids Res. 27:260-262; and Sonnhammer, et al. (1998) Nuc. Acids Res. 26:320-322.

In another embodiment, the prostate cancer sequences are transmembrane proteins. Transmembrane proteins are molecules that span a phospholipid bilayer of a cell. They may have an intracellular domain, an extracellular domain, or both. The intracellular domains of such proteins may have a number of functions including those already described for intracellular proteins. For example, the intracellular domain may have enzymatic activity and/or may serve as a binding site for additional proteins. Frequently the intracellular domain of transmembrane proteins serves both roles. For example certain receptor tyrosine kinases have both protein kinase activity and SH2 domains. In addition, autophosphorylation of tyrosines on the receptor molecule itself, creates binding sites for additional SH2 domain containing proteins.

Transmembrane proteins may contain from one to many transmembrane domains. For example, receptor tyrosine kinases, certain cytokine receptors, receptor guanylyl cyclases and receptor serine/threonine protein kinases contain a single transmembrane domain. However, various other proteins including channels and adenylyl cyclases contain numerous

transmembrane domains. Many important cell surface receptors such as G protein coupled receptors (GPCRs) are classified as “seven transmembrane domain” proteins, as they contain 7 membrane spanning regions. Characteristics of transmembrane domains include approximately 17 consecutive hydrophobic amino acids that may be followed by charged amino acids. Therefore, upon analysis of the amino acid sequence of a particular protein, the localization and number of transmembrane domains within the protein may be predicted (see, e.g., PSORT web site <http://psort.nibb.ac.jp/>). Important transmembrane protein receptors include, but are not limited to the insulin receptor, insulin-like growth factor receptor, human growth hormone receptor, glucose transporters, transferrin receptor, epidermal growth factor receptor, low density lipoprotein receptor, epidermal growth factor receptor, leptin receptor, and interleukin receptors, e.g., IL-1 receptor, IL-2 receptor, etc.

The extracellular domains of transmembrane proteins are diverse; however, conserved motifs are found repeatedly among various extracellular domains. Conserved structure and/or functions have been ascribed to different extracellular motifs. Many extracellular domains are involved in binding to other molecules. In one aspect, extracellular domains are found on receptors. Factors that bind the receptor domain include circulating ligands, which may be peptides, proteins, or small molecules such as adenosine and the like. For example, growth factors such as EGF, FGF, and PDGF are circulating growth factors that bind to their cognate receptors to initiate a variety of cellular responses. Other factors include cytokines, mitogenic factors, neurotrophic factors and the like. Extracellular domains also bind to cell-associated molecules. In this respect, they mediate cell-cell interactions. Cell-associated ligands can be tethered to the cell, e.g., via a glycosylphosphatidylinositol (GPI) anchor, or may themselves be transmembrane proteins. Extracellular domains also associate with the extracellular matrix and contribute to the maintenance of the cell structure.

Prostate cancer proteins that are transmembrane are particularly preferred in the present invention as they are readily accessible targets for immunotherapeutics, as are described herein. In addition, as outlined below, transmembrane proteins can be also useful in imaging modalities. Antibodies may be used to label such readily accessible proteins in situ. Alternatively, antibodies can also label intracellular proteins, in which case samples are typically permeabilized to provide access to intracellular proteins.. In addition, some membrane proteins can be processed to release a soluble protein, or to expose a residual

fragment. Released soluble proteins may be useful diagnostic markers, processed residual protein fragments may be useful prostate markers of disease.

It will also be appreciated by those in the art that a transmembrane protein can be made soluble by removing transmembrane sequences, e.g., through recombinant methods.

5 Furthermore, transmembrane proteins that have been made soluble can be made to be secreted through recombinant means by adding an appropriate signal sequence.

In another embodiment, the prostate cancer proteins are secreted proteins; the secretion of which can be either constitutive or regulated. These proteins may have a signal peptide or signal sequence that targets the molecule to the secretory pathway. Secreted
10 proteins are involved in numerous physiological events; by virtue of their circulating nature, they often serve to transmit signals to various other cell types. The secreted protein may function in an autocrine manner (acting on the cell that secreted the factor), a paracrine manner (acting on cells in close proximity to the cell that secreted the factor), an endocrine manner (acting on cells at a distance, e.g., secretion into the blood stream), or an exocrine
15 manner (secretion, e.g., through a duct or to adjacent epithelial surface as sweat glands, sebaceous glands, pancreatic ducts, lacrimal glands, mammary glands, salivary glands of the ear, etc.). Thus secreted molecules find use in modulating or altering numerous aspects of physiology. Prostate cancer proteins that are secreted proteins are particularly preferred in the present invention as they serve as good targets for diagnostic markers, e.g., for blood,
20 plasma, serum, or stool tests. Those which are enzymes may be antibody or small molecule targets. Others may be useful as vaccine targets, e.g., via CTL mechanisms.

Use of prostate cancer nucleic acids

As described above, prostate cancer sequence is initially identified by substantial
25 nucleic acid and/or amino acid sequence homology or linkage to the prostate cancer sequences outlined herein. Such homology can be based upon the overall nucleic acid or amino acid sequence, and is generally determined as outlined below, using either homology programs or hybridization conditions. Typically, linked sequences on a mRNA are found on the same molecule.

30 The prostate cancer nucleic acid sequences of the invention, e.g., the sequences in Tables 1A-4, can be fragments of larger genes, i.e., they are nucleic acid segments. "Genes" in this context includes coding regions, non-coding regions, and mixtures of coding and non-

coding regions. Accordingly, as will be appreciated by those in the art, using the sequences provided herein, extended sequences, in either direction, of the prostate cancer genes can be obtained, using techniques well known in the art for cloning either longer sequences or the full length sequences; see Ausubel, et al., supra. Much can be done by informatics and many
5 sequences can be clustered to include multiple sequences corresponding to a single gene, e.g., systems such as UniGene (see, <http://www.ncbi.nlm.nih.gov/UniGene/>).

Once the prostate cancer nucleic acid is identified, it can be cloned and, if necessary, its constituent parts recombined to form the entire prostate cancer nucleic acid coding regions or the entire mRNA sequence. Once isolated from its natural source, e.g., contained within a
10 plasmid or other vector or excised therefrom as a linear nucleic acid segment, the recombinant prostate cancer nucleic acid can be further-used as a probe to identify and isolate other prostate cancer nucleic acids, e.g., extended coding regions. It can also be used as a “precursor” nucleic acid to make modified or variant prostate cancer nucleic acids and proteins.

15 The prostate cancer nucleic acids of the present invention are used in several ways. In a first embodiment, nucleic acid probes to the prostate cancer nucleic acids are made and attached to biochips to be used in screening and diagnostic methods, as outlined below, or for administration, e.g., for gene therapy, vaccine, and/or antisense applications. Alternatively, the prostate cancer nucleic acids that include coding regions of prostate cancer proteins can
20 be put into expression vectors for the expression of prostate cancer proteins, again for screening purposes or for administration to a patient.

In a preferred embodiment, nucleic acid probes to prostate cancer nucleic acids (both the nucleic acid sequences outlined in the figures and/or the complements thereof) are made. The nucleic acid probes attached to the biochip are designed to be substantially
25 complementary to the prostate cancer nucleic acids, i.e., the target sequence (either the target sequence of the sample or to other probe sequences, e.g., in sandwich assays), such that hybridization of the target sequence and the probes of the present invention occurs. As outlined below, this complementarity need not be perfect; there may be base pair mismatches which will interfere with hybridization between the target sequence and the single stranded
30 nucleic acids of the present invention. However, if the number of mutations is so great that no hybridization can occur under even the least stringent of hybridization conditions, the sequence is not a complementary target sequence. Thus, by “substantially complementary”

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herein is meant that the probes are sufficiently complementary to the target sequences to hybridize under normal reaction conditions, particularly high stringency conditions, as outlined herein.

A nucleic acid probe is generally single stranded but can be partially single and
5 partially double stranded. The strandedness of the probe is dictated by the structure, composition, and properties of the target sequence. In general, the nucleic acid probes range from about 8 to about 100 bases long, with from about 10 to about 80 bases being preferred, and from about 30 to about 50 bases being particularly preferred. That is, generally whole genes are not used. In some embodiments, much longer nucleic acids can be used, up to
10 hundreds of bases.

In a preferred embodiment, more than one probe per sequence is used, with either overlapping probes or probes to different sections of the target being used. That is, two, three, four or more probes, with three being preferred, are used to build in a redundancy for a particular target. The probes can be overlapping (i.e., have some sequence in common), or
15 separate. In some cases, PCR primers may be used to amplify signal for higher sensitivity.

As will be appreciated by those in the art, nucleic acids can be attached or immobilized to a solid support in a wide variety of ways. By "immobilized" and grammatical equivalents herein is meant the association or binding between the nucleic acid probe and the solid support is sufficient to be stable under the conditions of binding, washing, analysis, and
20 removal as outlined below. The binding can typically be covalent or non-covalent. By "non-covalent binding" and grammatical equivalents herein is meant one or more of electrostatic, hydrophilic, and hydrophobic interactions. Included in non-covalent binding is the covalent attachment of a molecule, such as, streptavidin to the support and the non-covalent binding of the biotinylated probe to the streptavidin. By "covalent binding" and grammatical
25 equivalents herein is meant that the two moieties, the solid support and the probe, are attached by at least one bond, including sigma bonds, pi bonds and coordination bonds. Covalent bonds can be formed directly between the probe and the solid support or can be formed by a cross linker or by inclusion of a specific reactive group on either the solid support or the probe or both molecules. Immobilization may also involve a combination of
30 covalent and non-covalent interactions.

In general, the probes are attached to the biochip in a wide variety of ways, as will be appreciated by those in the art. As described herein, the nucleic acids can either be

synthesized first, with subsequent attachment to the biochip, or can be directly synthesized on the biochip.

The biochip comprises a suitable solid substrate. By "substrate" or "solid support" or other grammatical equivalents herein is meant a material that can be modified to contain discrete individual sites appropriate for the attachment or association of the nucleic acid probes and is amenable to at least one detection method. As will be appreciated by those in the art, the number of possible substrates are very large, and include, but are not limited to, glass and modified or functionalized glass, plastics (including acrylics, polystyrene and copolymers of styrene and other materials, polypropylene, polyethylene, polybutylene, polyurethanes, Teflon, etc.), polysaccharides, nylon or nitrocellulose, resins, silica or silica-based materials including silicon and modified silicon, carbon, metals, inorganic glasses, plastics, etc. In general, the substrates allow optical detection and do not appreciably fluoresce. A preferred substrate is described in WO0055627, herein incorporated by reference in its entirety.

Generally the substrate is planar, although as will be appreciated by those in the art, other configurations of substrates may be used as well. For example, the probes may be placed on the inside surface of a tube, for flow-through sample analysis to minimize sample volume. Similarly, the substrate may be flexible, such as a flexible foam, including closed cell foams made of particular plastics.

In a preferred embodiment, the surface of the biochip and the probe may be derivatized with chemical functional groups for subsequent attachment of the two. Thus, e.g., the biochip is derivatized with a chemical functional group including, but not limited to, amino groups, carboxy groups, oxo groups and thiol groups, with amino groups being particularly preferred. Using these functional groups, the probes can be attached using functional groups on the probes. For example, nucleic acids containing amino groups can be attached to surfaces comprising amino groups, e.g., using linkers as are known in the art; e.g., homo- or hetero-bifunctional linkers as are well known (see 1994 Pierce Chemical Company catalog, technical section on cross-linkers, pages 155-200). In addition, in some cases, additional linkers, such as alkyl groups (including substituted and heteroalkyl groups) may be used.

In this embodiment, oligonucleotides are synthesized as is known in the art, and then attached to the surface of the solid support. As will be appreciated by those skilled in the art,

either the 5' or 3' terminus may be attached to the solid support, or attachment may be via an internal nucleoside.

In another embodiment, the immobilization to the solid support may be very strong, yet non-covalent. For example, biotinylated oligonucleotides can be made, which bind to
5 surfaces covalently coated with streptavidin, resulting in attachment.

Alternatively, the oligonucleotides may be synthesized on the surface, as is known in the art. For example, photoactivation techniques utilizing photopolymerization compounds and techniques are used. In a preferred embodiment, the nucleic acids can be synthesized in situ, using well known photolithographic techniques, such as those described in WO
10 95/25116; WO 95/35505; U.S. Patent Nos. 5,700,637 and 5,445,934; and references cited within, all of which are expressly incorporated by reference; these methods of attachment form the basis of the Affymetrix GeneChip™ technology.

Often, amplification-based assays are performed to measure the expression level of prostate cancer-associated sequences. These assays are typically performed in conjunction
15 with reverse transcription. In such assays, a prostate cancer-associated nucleic acid sequence acts as a template in an amplification reaction (e.g., Polymerase Chain Reaction, or PCR). In a quantitative amplification, the amount of amplification product will be proportional to the amount of template in the original sample. Comparison to appropriate controls provides a measure of the amount of prostate cancer-associated RNA. Methods of quantitative
20 amplification are well known to those of skill in the art. Detailed protocols for quantitative PCR are provided, e.g., in Innis, et al. (1990) PCR Protocols: A Guide to Methods and Applications Academic Press.

In some embodiments, a TaqMan based assay is used to measure expression. TaqMan based assays use a fluorogenic oligonucleotide probe that contains a 5' fluorescent
25 dye and a 3' quenching agent. The probe hybridizes to a PCR product, but cannot itself be extended due to a blocking agent at the 3' end. When the PCR product is amplified in subsequent cycles, the 5' nuclease activity of the polymerase, e.g., AmpliTaq, results in the cleavage of the TaqMan probe. This cleavage separates the 5' fluorescent dye and the 3' quenching agent, thereby resulting in an increase in fluorescence as a function of
30 amplification (see, e.g., literature provided by Perkin-Elmer, e.g., www2.perkin-elmer.com).

Other suitable amplification methods include, but are not limited to, ligase chain reaction (LCR) (see Wu and Wallace (1989) Genomics 4:560-569, Landegren, et al. (1988)

Science 241:1077-1080, and Barringer, et al. (1990) Gene 89:117-122), transcription amplification (Kwoh, et al. (1989) Proc. Natl. Acad. Sci. USA 86:1173-1177), self-sustained sequence replication (Guatelli, et al. (1990) Proc. Nat. Acad. Sci. USA 87:1874-1878), dot PCR, and linker adapter PCR, etc.

5

Expression of prostate cancer proteins from nucleic acids

In a preferred embodiment, prostate cancer nucleic acids, e.g., encoding prostate cancer proteins are used to make a variety of expression vectors to express prostate cancer proteins which can then be used in screening assays, as described below. Expression vectors and recombinant DNA technology are well known to those of skill in the art (see, e.g., Ausubel, supra, and Fernandez and Hoeffler (eds. 1999) Gene Expression Systems Academic Press) and are used to express proteins. The expression vectors may be either self-replicating extrachromosomal vectors or vectors which integrate into a host genome. Generally, these expression vectors include transcriptional and translational regulatory nucleic acid operably linked to the nucleic acid encoding the prostate cancer protein. The term "control sequences" refers to DNA sequences used for the expression of an operably linked coding sequence in a particular host organism. Control sequences that are suitable for prokaryotes, e.g., include a promoter, optionally an operator sequence, and a ribosome binding site. Eukaryotic cells are known to utilize promoters, polyadenylation signals, and enhancers.

Nucleic acid is "operably linked" when it is placed into a functional relationship with another nucleic acid sequence. For example, DNA for a presequence or secretory leader is operably linked to DNA for a polypeptide if it is expressed as a preprotein that participates in the secretion of the polypeptide; a promoter or enhancer is operably linked to a coding sequence if it affects the transcription of the sequence; a ribosome binding site is operably linked to a coding sequence if it is positioned so as to facilitate translation, and sequences may be operably linked when they are physically linked on the same molecule. Generally, "operably linked" means that the DNA sequences being linked are contiguous, and, in the case of a secretory leader, contiguous and in reading phase. However, enhancers do not have to be contiguous. Linking is typically accomplished by ligation at convenient restriction sites. If such sites do not exist, synthetic oligonucleotide adaptors or linkers are used in accordance with conventional practice. Transcriptional and translational regulatory nucleic acid will generally be appropriate to the host cell used to express the prostate cancer protein.

Numerous types of appropriate expression vectors, and suitable regulatory sequences are known in the art for a variety of host cells.

In general, transcriptional and translational regulatory sequences may include, but are not limited to, promoter sequences, ribosomal binding sites, transcriptional start and stop
5 sequences, translational start and stop sequences, and enhancer or activator sequences. In a preferred embodiment, the regulatory sequences include a promoter and transcriptional start and stop sequences.

Promoter sequences encode either constitutive or inducible promoters. The promoters may be either naturally occurring promoters or hybrid promoters. Hybrid promoters, which
10 combine elements of more than one promoter, are also known in the art, and are useful in the present invention.

In addition, an expression vector may comprise additional elements. For example, the expression vector may have two replication systems, thus allowing it to be maintained in two organisms, e.g., in mammalian or insect cells for expression and in a prokaryotic host for
15 cloning and amplification. Furthermore, for integrating expression vectors, the expression vector contains at least one sequence homologous to the host cell genome, and preferably two homologous sequences which flank the expression construct. The integrating vector may be directed to a specific locus in the host cell by selecting the appropriate homologous sequence for inclusion in the vector. Constructs for integrating vectors are well known in the art (e.g.,
20 Fernandez and Hoeffler, supra).

In addition, in a preferred embodiment, the expression vector contains a selectable marker gene to allow the selection of transformed host cells. Selection genes are well known in the art and will vary with the host cell used.

The prostate cancer proteins of the present invention are produced by culturing a host
25 cell transformed with an expression vector containing nucleic acid encoding a prostate cancer protein, under the appropriate conditions to induce or cause expression of the prostate cancer protein. Conditions appropriate for prostate cancer protein expression will vary with the choice of the expression vector and the host cell, and will be easily ascertained by one skilled in the art through routine experimentation or optimization. For example, the use of
30 constitutive promoters in the expression vector will require optimizing the growth and proliferation of the host cell, while the use of an inducible promoter requires the appropriate growth conditions for induction. In addition, in some embodiments, the timing of the harvest

is important. For example, the baculoviral systems used in insect cell expression are lytic viruses, and thus harvest time selection can be crucial for product yield.

Appropriate host cells include yeast, bacteria, archaebacteria, fungi, and insect and animal cells, including mammalian cells. Of particular interest are *Saccharomyces cerevisiae* and other yeasts, *E. coli*, *Bacillus subtilis*, Sf9 cells, C129 cells, 293 cells, *Neurospora*, BHK, CHO, COS, HeLa cells, HUVEC (human umbilical vein endothelial cells), THP1 cells (a macrophage cell line) and various other human cells and cell lines.

In a preferred embodiment, the prostate cancer proteins are expressed in mammalian cells. Mammalian expression systems are also known in the art, and include retroviral and adenoviral systems. One expression vector system is a retroviral vector system such as is generally described in PCT/US97/01019 and PCT/US97/01048, both of which are hereby expressly incorporated by reference. Of particular use as mammalian promoters are the promoters from mammalian viral genes, since the viral genes are often highly expressed and have a broad host range. Examples include the SV40 early promoter, mouse mammary tumor virus LTR promoter, adenovirus major late promoter, herpes simplex virus promoter, and the CMV promoter (see, e.g., Fernandez and Hoeffler, supra). Typically, transcription termination and polyadenylation sequences recognized by mammalian cells are regulatory regions located 3' to the translation stop codon and thus, together with the promoter elements, flank the coding sequence. Examples of transcription terminator and polyadenylation signals include those derived from SV40.

The methods of introducing exogenous nucleic acid into mammalian hosts, as well as other hosts, is well known in the art, and will vary with the host cell used. Techniques include dextran-mediated transfection, calcium phosphate precipitation, polybrene mediated transfection, protoplast fusion, electroporation, viral infection, encapsulation of the polynucleotide(s) in liposomes, and direct microinjection of the DNA into nuclei.

In a preferred embodiment, prostate cancer proteins are expressed in bacterial systems. Bacterial expression systems are well known in the art. Promoters from bacteriophage may also be used and are known in the art. In addition, synthetic promoters and hybrid promoters are also useful; e.g., the *tac* promoter is a hybrid of the *trp* and *lac* promoter sequences. Furthermore, a bacterial promoter can include naturally occurring promoters of non-bacterial origin that have the ability to bind bacterial RNA polymerase and initiate transcription. In addition to a functioning promoter sequence, an efficient ribosome

binding site is desirable. The expression vector may also include a signal peptide sequence that provides for secretion of the prostate cancer protein in bacteria. The protein is either secreted into the growth media (gram-positive bacteria) or into the periplasmic space, located between the inner and outer membrane of the cell (gram-negative bacteria). The bacterial
5 expression vector may also include a selectable marker gene to allow for the selection of bacterial strains that have been transformed. Suitable selection genes include genes which render the bacteria resistant to drugs such as ampicillin, chloramphenicol, erythromycin, kanamycin, neomycin and tetracycline. Selectable markers also include biosynthetic genes, such as those in the histidine, tryptophan and leucine biosynthetic pathways. These
10 components are assembled into expression vectors. Expression vectors for bacteria are well known in the art, and include vectors for *Bacillus subtilis*, *E. coli*, *Streptococcus cremoris*, and *Streptococcus lividans*, among others (e.g., Fernandez and Hoeffler, *supra*). The bacterial expression vectors are transformed into bacterial host cells using techniques well known in the art, such as calcium chloride treatment, electroporation, and others.

15 In one embodiment, prostate cancer proteins are produced in insect cells. Expression vectors for the transformation of insect cells, and in particular, baculovirus-based expression vectors, are well known in the art.

In a preferred embodiment, prostate cancer protein is produced in yeast cells. Yeast expression systems are well known in the art, and include expression vectors for
20 *Saccharomyces cerevisiae*, *Candida albicans* and *C. maltosa*, *Hansenula polymorpha*, *Kluyveromyces fragilis* and *K. lactis*, *Pichia guillerimondii* and *P. pastoris*, *Schizosaccharomyces pombe*, and *Yarrowia lipolytica*.

The prostate cancer protein may also be made as a fusion protein, using techniques well known in the art. Thus, e.g., for the creation of monoclonal antibodies, if the desired
25 epitope is small, the prostate cancer protein may be fused to a carrier protein to form an immunogen. Alternatively, the prostate cancer protein may be made as a fusion protein to increase expression, or for other reasons. For example, when the prostate cancer protein is a prostate cancer peptide, the nucleic acid encoding the peptide may be linked to other nucleic acid for expression purposes.

30 In a preferred embodiment, the prostate cancer protein is purified or isolated after expression. Prostate cancer proteins may be isolated or purified in a variety of ways known to those skilled in the art depending on what other components are present in the sample.

Standard purification methods include electrophoretic, molecular, immunological and chromatographic techniques, including ion exchange, hydrophobic, affinity, and reverse-phase HPLC chromatography, and chromatofocusing. For example, the prostate cancer protein may be purified using a standard anti-prostate cancer protein antibody column.

- 5 Ultrafiltration and diafiltration techniques, in conjunction with protein concentration, are also useful. For general guidance in suitable purification techniques, see Scopes (1982) Protein Purification Springer-Verlag. The degree of purification necessary will vary depending on the use of the prostate cancer protein. In some instances no purification will be necessary.

- 10 Once expressed and purified if necessary, the prostate cancer proteins and nucleic acids are useful in a number of applications. They may be used as immunoselection reagents, as vaccine reagents, as screening agents, etc.

Variants of prostate cancer proteins

- 15 In one embodiment, the prostate cancer proteins are derivative or variant prostate cancer proteins as compared to the wild-type sequence. That is, as outlined more fully below, the derivative prostate cancer peptide will often contain at least one amino acid substitution, deletion or insertion, with amino acid substitutions being particularly preferred. The amino acid substitution, insertion, or deletion may occur at most any residue within the prostate cancer peptide.

- 20 Also included within one embodiment of prostate cancer proteins of the present invention are amino acid sequence variants. These variants typically fall into one or more of three classes: substitutional, insertional, or deletional variants. These variants ordinarily are prepared by site specific mutagenesis of nucleotides in the DNA encoding the prostate cancer protein, using cassette or PCR mutagenesis or other techniques well known in the art, to
25 produce DNA encoding the variant, and thereafter expressing the DNA in recombinant cell culture as outlined above. However, variant prostate cancer protein fragments having up to about 100-150 residues may be prepared by in vitro synthesis using established techniques. Amino acid sequence variants are characterized by the predetermined nature of the variation, a feature that sets them apart from naturally occurring allelic or interspecies variation of the
30 prostate cancer protein amino acid sequence. The variants typically exhibit the same qualitative biological activity as the naturally occurring analogue, although variants can also be selected which have modified characteristics as will be more fully outlined below.

While the site or region for introducing an amino acid sequence variation is predetermined, the mutation per se need not be predetermined. For example, in order to optimize the performance of a mutation at a given site, random mutagenesis may be conducted at the target codon or region and the expressed prostate cancer variants screened
5 for the optimal combination of desired activity. Techniques for making substitution mutations at predetermined sites in DNA having a known sequence are well known, e.g., M13 primer mutagenesis and PCR mutagenesis. Screening of the mutants is done using assays of prostate cancer protein activities.

Amino acid substitutions are typically of single residues; insertions usually will be on
10 the order of from about 1 to 20 amino acids, although considerably larger insertions may be tolerated. Deletions range from about 1 to about 20 residues, although in some cases deletions may be much larger.

Substitutions, deletions, insertions or a combination thereof may be used to arrive at a final derivative. Generally these changes are done on a few amino acids to minimize the
15 alteration of the molecule. However, larger changes may be tolerated in certain circumstances. When small alterations in the characteristics of the prostate cancer protein are desired, substitutions are generally made in accordance with the amino acid substitution relationships provided in the definition section.

The variants typically exhibit the same qualitative biological activity and will elicit
20 the same immune response as the naturally-occurring analog, although variants also are selected to modify the characteristics of the prostate cancer proteins as needed. Alternatively, the variant may be designed such that the biological activity of the prostate cancer protein is altered. For example, glycosylation sites may be altered or removed.

Substantial changes in function or immunological identity are made by selecting
25 substitutions that are less conservative than those described above. For example, substitutions may be made which more significantly affect: the structure of the polypeptide backbone in the area of the alteration, for example the alpha-helical or beta-sheet structure; the charge or hydrophobicity of the molecule at the target site; or the bulk of the side chain. The substitutions which in general are expected to produce the greatest changes in the
30 polypeptide's properties are those in which (a) a hydrophilic residue, e.g., serinyl or threoninyl is substituted for (or by) a hydrophobic residue, e.g., leucyl, isoleucyl, phenylalanyl, valyl or alanyl; (b) a cysteine or proline is substituted for (or by) another residue; (c) a residue having

an electropositive side chain, e.g., lysyl, arginyl, or histidyl, is substituted for (or by) an electronegative residue, e.g., glutamyl or aspartyl; or (d) a residue having a bulky side chain, e.g., phenylalanine, is substituted for (or by) one not having a side chain, e.g., glycine.

Covalent modifications of prostate cancer polypeptides are included within the scope of this invention. One type of covalent modification includes reacting targeted amino acid residues of a prostate cancer polypeptide with an organic derivatizing agent that is capable of reacting with selected side chains or the N-or C-terminal residues of a prostate cancer polypeptide. Derivatization with bifunctional agents is useful, for instance, for crosslinking prostate cancer polypeptides to a water-insoluble support matrix or surface for use in the method for purifying anti-prostate cancer polypeptide antibodies or screening assays, as is more fully described below. Commonly used crosslinking agents include, e.g., 1,1-bis(diazoacetyl)-2-phenylethane, glutaraldehyde, N-hydroxysuccinimide esters, e.g., esters with 4-azidosalicylic acid, homobifunctional imidoesters, including disuccinimidyl esters such as 3,3'-dithiobis(succinimidylpropionate), bifunctional maleimides such as bis-N-maleimido-1,8-octane and agents such as methyl-3-((p-azidophenyl)dithio)propioimide.

Other modifications include deamidation of glutaminyl and asparaginyl residues to the corresponding glutamyl and aspartyl residues, respectively, hydroxylation of proline and lysine, phosphorylation of hydroxyl groups of serinyl, threonyl or tyrosyl residues, methylation of the amino groups of the lysine, arginine, and histidine side chains (e.g., pp. 79-86, Creighton (1983) Proteins: Structure and Molecular Properties Freeman), acetylation of the N-terminal amine, and amidation of a C-terminal carboxyl group.

Another type of covalent modification of the prostate cancer polypeptide included within the scope of this invention comprises altering the native glycosylation pattern of the polypeptide. "Altering the native glycosylation pattern" is intended for purposes herein to mean deleting one or more carbohydrate moieties found in native sequence prostate cancer polypeptide, and/or adding one or more glycosylation sites that are not present in the native sequence prostate cancer polypeptide. Glycosylation patterns can be altered in many ways. For example the use of different cell types to express prostate cancer-associated sequences can result in different glycosylation patterns.

Addition of glycosylation sites to prostate cancer polypeptides may also be accomplished by altering the amino acid sequence thereof. The alteration may be made, e.g., by the addition of, or substitution by, one or more serine or threonine residues to the native

sequence prostate cancer polypeptide (for O-linked glycosylation sites). The prostate cancer amino acid sequence may optionally be altered through changes at the DNA level, particularly by mutating the DNA encoding the prostate cancer polypeptide at preselected bases such that codons are generated that will translate into the desired amino acids.

5 Another means of increasing the number of carbohydrate moieties on the prostate cancer polypeptide is by chemical or enzymatic coupling of glycosides to the polypeptide. Such methods are described in the art, e.g., in WO 87/05330, and pp. 259-306 in Aplin and Wriston (1981) CRC Crit. Rev. Biochem.

10 Removal of carbohydrate moieties present on the prostate cancer polypeptide may be accomplished chemically or enzymatically or by mutational substitution of codons encoding for amino acid residues that serve as targets for glycosylation. Chemical deglycosylation techniques are known in the art and described, e.g., by Hakimuddin, et al. (1987) Arch. Biochem. Biophys. 259:52-57; and Edge, et al. (1981) Anal. Biochem. 118:131-137. Enzymatic cleavage of carbohydrate moieties on polypeptides can be achieved by the use of a
15 variety of endo-and exo-glycosidases as described by Thotakura, et al. (1987) Meth. Enzymol. 138:350-359.

20 Another type of covalent modification of prostate cancer comprises linking the prostate cancer polypeptide to one of a variety of nonproteinaceous polymers, e.g., polyethylene glycol, polypropylene glycol, or polyoxyalkylenes, in the manner set forth in U.S. Patent Nos. 4,640,835; 4,496,689; 4,301,144; 4,670,417; 4,791,192; or 4,179,337.

25 Prostate cancer polypeptides of the present invention may also be modified in a way to form chimeric molecules comprising a prostate cancer polypeptide fused to another, heterologous polypeptide or amino acid sequence. In one embodiment, such a chimeric molecule comprises a fusion of a prostate cancer polypeptide with a tag polypeptide which provides an epitope to which an anti-tag antibody can selectively bind. The epitope tag is generally placed at the amino-or carboxyl-terminus of the prostate cancer polypeptide. The presence of such epitope-tagged forms of a prostate cancer polypeptide can be detected using an antibody against the tag polypeptide. Also, provision of the epitope tag enables the prostate cancer polypeptide to be readily purified by affinity purification using an anti-tag
30 antibody or another type of affinity matrix that binds to the epitope tag. In an alternative embodiment, the chimeric molecule may comprise a fusion of a prostate cancer polypeptide

with an immunoglobulin or a particular region of an immunoglobulin. For a bivalent form of the chimeric molecule, such a fusion could be to the Fc region of an IgG molecule.

Various tag polypeptides and their respective antibodies are well known in the art. Examples include poly-histidine (poly-his) or poly-histidine-glycine (poly-his-gly) tags; HIS6
5 and metal chelation tags, the flu HA tag polypeptide and its antibody 12CA5 (Field, et al. (1988) Mol. Cell. Biol. 8:2159-2165; the c-myc tag and the 8F9, 3C7, 6E10, G4, B7, and 9E10 antibodies thereto (Evan, et al. (1985) Molecular and Cellular Biology 5:3610-3616); and the Herpes Simplex virus glycoprotein D (gD) tag and its antibody (Paborsky, et al. (1990) Protein Engineering 3:547-553). Other tag polypeptides include the Flag-peptide
10 (Hopp, et al. (1988) BioTechnology 6:1204-1210); the KT3 epitope peptide (Martin, et al. (1992) Science 255:192-194); tubulin epitope peptide (Skinner, et al. (1991) J. Biol. Chem. 266:15163-15166); and the T7 gene 10 protein peptide tag (Lutz-Freyermuth, et al. (1990) Proc. Natl. Acad. Sci. USA 87:6393-6397).

Also included are other prostate cancer proteins of the prostate cancer family, and
15 prostate cancer proteins from other organisms, which are cloned and expressed as outlined below. Thus, probe or degenerate polymerase chain reaction (PCR) primer sequences may be used to find other related prostate cancer proteins from humans or other organisms. As will be appreciated by those in the art, particularly useful probe and/or PCR primer sequences include the unique areas of the prostate cancer nucleic acid sequence. As is generally known
20 in the art, preferred PCR primers are from about 15 to about 35 nucleotides in length, with from about 20 to about 30 being preferred, and may contain inosine as needed. The conditions for the PCR reaction are well known in the art (e.g., Innis, PCR Protocols, supra).

Antibodies to prostate cancer proteins

25 In a preferred embodiment, when the prostate cancer protein is to be used to generate antibodies, e.g., for immunotherapy or immunodiagnosis, the prostate cancer protein should share at least one epitope or determinant with the full length protein. By "epitope" or "determinant" herein is typically meant a portion of a protein which will generate and/or bind an antibody or T-cell receptor in the context of MHC. Thus, in most instances, antibodies
30 made to a smaller prostate cancer protein will be able to bind to the full-length protein, particularly linear epitopes. In a preferred embodiment, the epitope is unique; that is, antibodies generated to a unique epitope show little or no cross-reactivity.

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Methods of preparing polyclonal antibodies are known to the skilled artisan (e.g., Coligan, supra; and Harlow and Lane, supra). Polyclonal antibodies can be raised in a mammal, e.g., by one or more injections of an immunizing agent and, if desired, an adjuvant. Typically, the immunizing agent and/or adjuvant will be injected in the mammal by multiple subcutaneous or intraperitoneal injections. The immunizing agent may include a protein encoded by a nucleic acid of the figures or fragment thereof or a fusion protein thereof. It may be useful to conjugate the immunizing agent to a protein known to be immunogenic in the mammal being immunized. Examples of such immunogenic proteins include but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. Examples of adjuvants which may be employed include Freund's complete adjuvant and MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate). The immunization protocol may be selected by one skilled in the art without undue experimentation.

The antibodies may, alternatively, be monoclonal antibodies. Monoclonal antibodies may be prepared using hybridoma methods, such as those described by Kohler and Milstein (1975) Nature 256:495. In a hybridoma method, a mouse, hamster, or other appropriate host animal, is typically immunized with an immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent. Alternatively, the lymphocytes may be immunized in vitro. The immunizing agent will typically include a polypeptide encoded by a nucleic acid of Tables 1A-4 or fragment thereof, or a fusion protein thereof. Generally, either peripheral blood lymphocytes ("PBLs") are used if cells of human origin are desired, or spleen cells or lymph node cells are used if non-human mammalian sources are desired. The lymphocytes are then fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell (see pp. 59-103 in Goding (1986) Monoclonal Antibodies: Principles and Practice Academic Press). Immortalized cell lines are usually transformed mammalian cells, particularly myeloma cells of rodent, bovine and human origin. Usually, rat or mouse myeloma cell lines are employed. The hybridoma cells may be cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium

for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine ("HAT medium"), which substances prevent the growth of HGPRT-deficient cells.

In one embodiment, the antibodies are bispecific antibodies. Bispecific antibodies are monoclonal, preferably human or humanized, antibodies that have binding specificities for at least two different antigens or that have binding specificities for two epitopes on the same antigen. In one embodiment, one of the binding specificities is for a protein encoded by a nucleic acid of Tables 1A-4 or a fragment thereof, the other one is for another antigen, and preferably for a cell-surface protein or receptor or receptor subunit, preferably one that is tumor specific. Alternatively, tetramer-type technology may create multivalent reagents.

In a preferred embodiment, the antibodies to prostate cancer protein are capable of reducing or eliminating a biological function of a prostate cancer protein, as is described below. That is, the addition of anti-prostate cancer protein antibodies (either polyclonal or preferably monoclonal) to prostate cancer tissue (or cells containing prostate cancer) may reduce or eliminate the prostate cancer. Generally, at least a 25% decrease in activity, growth, size or the like is preferred, with at least about 50% being particularly preferred and about a 95-100% decrease being especially preferred.

In a preferred embodiment the antibodies to the prostate cancer proteins are humanized antibodies (e.g., Xenerex Biosciences; Medarex, Inc.; Abgenix, Inc.; Protein Design Labs, Inc.). Humanized forms of non-human (e.g., murine) antibodies are chimeric molecules of immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab')₂ or other antigen-binding subsequences of antibodies) which contain minimal sequence derived from non-human immunoglobulin. Humanized antibodies include human immunoglobulins (recipient antibody) in which residues from a complementary determining region (CDR) of the recipient are replaced by residues from a CDR of a non-human species (donor antibody) such as mouse, rat or rabbit having the desired specificity, affinity and capacity. In some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human residues. Humanized antibodies may also comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. In general, a humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the framework (FR) regions are those of a human

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immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin (Jones, et al. (1986) Nature 321:522-525; Riechmann, et al. (1988) Nature 332:323-329; and Presta (1992) Curr. Op. Struct. Biol. 2:593-596). Humanization can be essentially performed following methods of Winter and co-workers (see, e.g., Jones, et al. (1986) Nature 321:522-525; Riechmann, et al. (1988) Nature 332:323-327; and Verhoeven, et al. (1988) Science 239:1534-1536), by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody. Accordingly, such humanized antibodies are chimeric antibodies (U.S. Patent No. 4,816,567), wherein substantially less than an intact human variable domain has been substituted by the corresponding sequence from a non-human species.

Human antibodies can also be produced using various techniques known in the art, including phage display libraries (Hoogenboom and Winter (1991) J. Mol. Biol. 227:381-388; Marks, et al. (1991) J. Mol. Biol. 222:581-597) or the preparation of human monoclonal antibodies (e.g., p77 in Cole, et al. (1985) Monoclonal Antibodies and Cancer Therapy Liss; and Boerner, et al. (1991) J. Immunol. 147(1):86-95). Similarly, human antibodies can be made by introducing of human immunoglobulin loci into transgenic animals, e.g., mice in which the endogenous immunoglobulin genes have been partially or completely inactivated. Upon challenge, human antibody production is observed, which closely resembles that seen in humans in most respects, including gene rearrangement, assembly, and antibody repertoire. This approach is described, e.g., in U.S. Patent Nos. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016, and in the following scientific publications: Marks, et al. (1992) Bio/Technology 10:779-783; Lonberg, et al. (1994) Nature 368:856-859; Morrison (1994) Nature 368:812-13; Fishwild, et al. (1996) Nature Biotechnology 14:845-51; Neuberger (1996) Nature Biotechnology 14:826; Lonberg and Huszar (1995) Intern. Rev. Immunol. 13:65-93.

By immunotherapy is meant treatment of prostate cancer with an antibody raised against prostate cancer proteins. As used herein, immunotherapy can be passive or active. Passive immunotherapy as defined herein is the passive transfer of antibody to a recipient (patient). Active immunization is the induction of antibody and/or T-cell responses in a recipient (patient). Induction of an immune response is the result of providing the recipient with an antigen to which antibodies are raised. As appreciated by one of ordinary skill in the

art, the antigen may be provided by injecting a polypeptide against which antibodies are desired to be raised into a recipient, or contacting the recipient with a nucleic acid capable of expressing the antigen and under conditions for expression of the antigen, leading to an immune response.

5 In a preferred embodiment the prostate cancer proteins against which antibodies are raised are secreted proteins as described above. Without being bound by theory, antibodies used for treatment, bind and prevent the secreted protein from binding to its receptor, thereby inactivating the secreted prostate cancer protein.

10 In another preferred embodiment, the prostate cancer protein to which antibodies are raised is a transmembrane protein. Without being bound by theory, antibodies used for treatment bind the extracellular domain of the prostate cancer protein and prevent it from binding to other proteins, such as circulating ligands or cell-associated molecules. The antibody may cause down-regulation of the transmembrane prostate cancer protein. As will be appreciated by one of ordinary skill in the art, the antibody may be a competitive, non-
15 competitive or uncompetitive inhibitor of protein binding to the extracellular domain of the prostate cancer protein. The antibody is also often an antagonist of the prostate cancer protein. Further, the antibody may prevent activation of the transmembrane prostate cancer protein. In one aspect, when the antibody prevents the binding of other molecules to the prostate cancer protein, the antibody prevents growth of the cell. The antibody may also be
20 used to target or sensitize the cell to cytotoxic agents, including, but not limited to TNF- α , TNF- β , IL-1, INF- γ , and IL-2, or chemotherapeutic agents including 5FU, vinblastine, actinomycin D, cisplatin, methotrexate, and the like. In some instances the antibody belongs to a sub-type that activates serum complement when complexed with the transmembrane protein thereby mediating cytotoxicity or antigen-dependent cytotoxicity (ADCC). Thus,
25 prostate cancer is treated by administering to a patient antibodies directed against the transmembrane prostate cancer protein. Antibody-labeling may activate a co-toxin, localize a toxin payload, or otherwise provide means to locally ablate cells.

 In another preferred embodiment, the antibody is conjugated to an effector moiety. The effector moiety can be a labeling moiety such as a radioactive label or fluorescent label,
30 or can be a therapeutic moiety. In one aspect the therapeutic moiety is a small molecule that modulates the activity of the prostate cancer protein. In another aspect the therapeutic moiety modulates the activity of molecules associated with or in close proximity to the prostate

cancer protein. The therapeutic moiety may inhibit enzymatic activity such as protease or collagenase or protein kinase activity associated with prostate cancer.

In a preferred embodiment, the therapeutic moiety can also be a cytotoxic agent. In this method, targeting the cytotoxic agent to prostate cancer tissue or cells, results in a reduction in the number of afflicted cells, thereby reducing symptoms associated with prostate cancer. Cytotoxic agents are numerous and varied and include, but are not limited to, cytotoxic drugs or toxins or active fragments of such toxins. Suitable toxins and their corresponding fragments include diphtheria A chain, exotoxin A chain, ricin A chain, abrin A chain, curcin, crotin, phenomycin, enomycin, saporin, auristatin, and the like. Cytotoxic agents also include radiochemicals made by conjugating radioisotopes to antibodies raised against prostate cancer proteins, or binding of a radionuclide to a chelating agent that has been covalently attached to the antibody. Targeting the therapeutic moiety to transmembrane prostate cancer proteins not only serves to increase the local concentration of therapeutic moiety in the prostate cancer afflicted area, but also serves to reduce deleterious side effects, e.g., by binding to normal tissues, that may be associated with the therapeutic moiety.

In another preferred embodiment, the prostate cancer protein against which the antibodies are raised is an intracellular protein. In this case, the antibody may be conjugated to a protein which facilitates entry into the cell. In one case, the antibody enters the cell by endocytosis. In another embodiment, a nucleic acid encoding the antibody is administered to the individual or cell. Moreover, wherein the prostate cancer protein can be targeted within a cell, i.e., the nucleus, an antibody thereto contains a signal for that target localization, i.e., a nuclear localization signal.

The prostate cancer antibodies of the invention specifically bind to prostate cancer proteins. By “specifically bind” herein is meant that the antibodies bind to the protein with a K_d of at least about 0.1 mM, more usually at least about 1 μ M, preferably at least about 0.1 μ M or better, and most preferably, 0.01 μ M or better. Selectivity of binding is also important.

Detection of prostate cancer sequence for diagnostic and therapeutic applications

In one aspect, the RNA expression levels of genes are determined for different cellular states in the prostate cancer phenotype. After androgen ablation therapy, cells that survive the therapy undergo a period of quiescence followed at sometime later by active cell

division. As explained above, there are a variety of expression patterns characteristic of the prostate cancer genes involved in androgen-independent prostate cancer. Some genes are expressed early in the time course following ablation therapy, then drop off in expression, and then express again with emergence of androgen-independence (hi-lo-hi pattern in 1A).

5 Other genes are expressed early in the time course following ablation therapy, then drop off in expression, and do not express again with emergence of androgen-independence (hi-lo-lo pattern in Table 1A). Still other genes are not expressed early in the time course, but express only with emergence of androgen-independence (lo-lo-hi pattern in Table 1A). Other genes are not expressed early in the time course, but then express as androgen is withdrawn and
10 continue to express with emergence of androgen-independence (lo-hi-hi pattern in Table 1A). Finally, some genes are not expressed early in the time course, but then express as androgen is withdrawn and drop off again with emergence of androgen-independence (lo-hi-lo pattern in Table 1A). Thus, the data suggest that different antigens are expressed in quiescent cells and actively dividing androgen-independent prostate cancer cells.

15 In another aspect, the RNA expression levels of genes are determined for different cellular states in the prostate cancer phenotype. After androgen ablation therapy, cells that survive the therapy undergo a period of quiescence followed at sometime later by active cell division. As explained above, there are a variety of expression patterns characteristic of the prostate cancer genes involved in androgen-independent prostate cancer. Some genes are
20 expressed early in the time course following ablation therapy, then drop off in expression, and then express again with emergence of androgen-independence (hi-lo-lo-hi pattern in Table 2A). Other genes are expressed early in the time course following ablation therapy, then drop off in expression, and do not express again with emergence of androgen-independence (hi-lo-lo-lo and hi-hi-lo-lo pattern in Table 2A). Still other genes are not
25 expressed early in the time course, but express only with emergence of androgen-independence (lo-lo-lo-hi pattern in Table 2A). Other genes are not expressed early in the time course, but then express as androgen is withdrawn and continue to express with emergence of androgen-independence (lo-lo-hi-hi pattern in Table 2A). Finally, some genes are not expressed early in the time course, but then express as androgen is withdrawn and
30 drop off again with emergence of androgen-independence (lo-lo-hi-lo pattern in Table 2A). Thus, the data suggest that different antigens are expressed in quiescent cells (during androgen withdrawal) and actively dividing androgen-independent prostate cancer cells.

Effective therapy to combat androgen-independent prostate cancer requires that the timing of therapy coincide with expression of the target genes. Patients can be monitored for the expression of certain diagnostic antigens that indicate the presence of quiescent cells or which indicate the transition to actively dividing androgen-independent prostate cancer cells.

5 Thus, therapy to combat androgen-independent prostate cancer should begin at some time following androgen ablation therapy, depending on the particular target. Typically the transition from quiescence to actively dividing androgen-independent prostate cancer occurs between 6-24 months following androgen ablation therapy. Thus, preferred time periods for the therapies of the invention are as follows:

10 Expression levels of genes in normal tissue (i.e., not undergoing prostate cancer) and in prostate cancer tissue (and in some cases, for varying severities of prostate cancer that relate to prognosis, as outlined below) or in non-malignant disease are evaluated to provide expression profiles. An expression profile of a particular cell state or point of development is essentially a "fingerprint" of the state. While two states may have a particular gene similarly
15 expressed, the evaluation of a number of genes simultaneously allows the generation of a gene expression profile that is reflective of the state of the cell. By comparing expression profiles of cells in different states, information regarding which genes are important (including both up- and down-regulation of genes) in each of these states is obtained. Then, diagnosis may be performed or confirmed to determine whether a tissue sample has the gene
20 expression profile of normal or cancerous tissue. This will provide for molecular diagnosis of related conditions.

"Differential expression," or grammatical equivalents as used herein, refers to qualitative or quantitative differences in the temporal and/or cellular gene expression patterns within and among cells and tissue. Thus, a differentially expressed gene can qualitatively
25 have its expression altered, including an activation or inactivation, in, e.g., normal versus prostate cancer tissue. Genes may be turned on or turned off in a particular state, relative to another state thus permitting comparison of two or more states. A qualitatively regulated gene will exhibit an expression pattern within a state or cell type which is detectable by standard techniques. Some genes will be expressed in one state or cell type, but not in both.
30 Alternatively, the difference in expression may be quantitative, e.g., in that expression is increased or decreased; i.e., gene expression is either upregulated, resulting in an increased amount of transcript, or downregulated, resulting in a decreased amount of transcript. The

degree to which expression differs need only be large enough to quantify via standard characterization techniques as outlined below, such as by use of Affymetrix GeneChip™ expression arrays, Lockhart (1996) Nature Biotechnology 14:1675-1680, hereby expressly incorporated by reference. Other techniques include, but are not limited to, quantitative reverse transcriptase PCR, northern analysis and RNase protection. As outlined above, preferably the change in expression (i.e., upregulation or downregulation) is at least about 50%, more preferably at least about 100%, more preferably at least about 150%, more preferably at least about 200%, with from 300 to at least 1000% being especially preferred.

Evaluation may be at the gene transcript, or the protein level. The amount of gene expression may be monitored using nucleic acid probes to the DNA or RNA equivalent of the gene transcript, and the quantification of gene expression levels, or, alternatively, the final gene product itself (protein) can be monitored, e.g., with antibodies to the prostate cancer protein and standard immunoassays (ELISAs, etc.) or other techniques, including mass spectroscopy assays, 2D gel electrophoresis assays, etc. Proteins corresponding to prostate cancer genes, i.e., those identified as being important in a prostate cancer or disease phenotype, can be evaluated in a prostate cancer diagnostic test.

In a preferred embodiment, gene expression monitoring is performed simultaneously on a number of genes. Multiple protein expression monitoring can be performed as well. Similarly, these assays may be performed on an individual basis as well.

In this embodiment, the prostate cancer nucleic acid probes are attached to biochips as outlined herein for the detection and quantification of prostate cancer sequences in a particular cell. The assays are further described below in the example. PCR techniques can be used to provide greater sensitivity.

In a preferred embodiment nucleic acids encoding the prostate cancer protein are detected. Although DNA or RNA encoding the prostate cancer protein may be detected, of particular interest are methods wherein an mRNA encoding a prostate cancer protein is detected. Probes to detect mRNA can be a nucleotide/deoxynucleotide probe that is complementary to and hybridizes with the mRNA and includes, but is not limited to, oligonucleotides, cDNA, or RNA. Probes also should contain a detectable label, as defined herein. In one method the mRNA is detected after immobilizing the nucleic acid to be examined on a solid support such as nylon membranes and hybridizing the probe with the sample. Following washing to remove the non-specifically bound probe, the label is

detected. In another method detection of the mRNA is performed in situ (in situ hybridization or ISH). In this method permeabilized cells or tissue samples are contacted with a detectably labeled nucleic acid probe for sufficient time to allow the probe to hybridize with the target mRNA. Following washing to remove the non-specifically bound probe, the label is detected. For example a digoxigenin labeled riboprobe (RNA probe) that is complementary to the mRNA encoding a prostate cancer protein is detected by binding the digoxigenin with an anti-digoxigenin secondary antibody and developed with nitro blue tetrazolium and 5-bromo-4-chloro-3-indoyl phosphate.

In a preferred embodiment, various proteins from the three classes of proteins as described herein (secreted, transmembrane, or intracellular proteins) are used in diagnostic assays. The prostate cancer proteins, antibodies, nucleic acids, modified proteins and cells containing prostate cancer sequences are used in diagnostic assays. Such may evaluate tissues, e.g., immunohistochemistry, or evaluate body fluids, e.g., blood. The detection may be direct of cells, or indirect, e.g., of products from cells. This can be performed on an individual gene or corresponding polypeptide level. In a preferred embodiment, the expression profiles are used, preferably in conjunction with high throughput screening techniques to allow monitoring for expression profile genes and/or corresponding polypeptides.

As described and defined herein, prostate cancer proteins, including intracellular, transmembrane, or secreted proteins, find use as prognostic or diagnostic markers of prostate cancer or other prostate conditions. Detection of these proteins in putative prostate cancer tissue allows for detection, diagnosis, or prognosis of prostate proliferative disorders (malignant and non-malignant) including benign prostate hyperplasia (BPH) and cancer, and prostatitis. Diagnosis may also assist in selecting a therapeutic strategy, e.g., based on expression profiles and/or comparison to archival samples. In one embodiment, antibodies are used to detect prostate cancer proteins, directly or indirectly. A preferred method separates proteins from a sample by electrophoresis on a gel (typically a denaturing and reducing protein gel, but may be another type of gel, including isoelectric focusing gels and the like). Following separation of proteins, the prostate cancer protein is detected, e.g., by immunoblotting with antibodies raised against the prostate cancer protein. Methods of immunoblotting are well known to those of ordinary skill in the art.

In another preferred method, antibodies to the prostate cancer protein find use in in situ imaging techniques, e.g., in histology and/or in immunohistochemistry (e.g., Asai (ed. 1993) Methods in Cell Biology: Antibodies in Cell Biology (vol. 37) Academic Press. In this method cells are contacted with from one to many antibodies to the prostate cancer protein(s).
5 Following washing to remove non-specific antibody binding, the presence of the antibody or antibodies is detected. In one embodiment the antibody is detected by incubating with a secondary antibody that contains a detectable label. In another method the primary antibody to the prostate cancer protein(s) contains a detectable label, e.g., an enzyme marker that can act on a substrate. In another preferred embodiment each one of multiple primary antibodies
10 contains a distinct and detectable label. This method finds particular use in simultaneous screening for a plurality of prostate cancer proteins. As will be appreciated by one of ordinary skill in the art, many other histological imaging techniques are also provided by the invention.

In a preferred embodiment the label is detected in a fluorometer which has the ability
15 to detect and distinguish emissions of different wavelengths. In addition, a fluorescence activated cell sorter (FACS) can be used in the method.

In another preferred embodiment, antibodies find use in diagnosing prostate cancer from blood, serum, plasma, stool, and other samples. Such samples, therefore, are useful as samples to be probed or tested for the presence of prostate cancer proteins, which may be
20 diagnostic of prostate conditions beyond cancer, e.g., BPH. Antibodies can be used to detect a prostate cancer protein by previously described immunoassay techniques including ELISA, immunoblotting (western blotting), immunoprecipitation, BIACORE technology, and the like. Conversely, the presence of antibodies may indicate an immune response against an endogenous prostate cancer protein.

25 In a preferred embodiment, in situ hybridization of labeled prostate cancer nucleic acid probes to tissue arrays is done. For example, arrays of tissue samples, including prostate cancer tissue and/or normal tissue, are made. In situ hybridization (see, e.g., Ausubel, supra) is then performed. When comparing the fingerprints between an individual and a standard, the skilled artisan can make a diagnosis, a prognosis, or a prediction based on the findings. It
30 is further understood that the genes which indicate the diagnosis may differ from those which indicate the prognosis and molecular profiling of the condition of the cells may lead to distinctions between responsive or refractory conditions or may be predictive of outcomes.

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In a preferred embodiment, the prostate cancer proteins, antibodies, nucleic acids, modified proteins, and cells containing prostate cancer sequences are used in prognosis assays. As above, gene expression profiles can be generated that correlate to prostate cancer or other prostate disorders, in terms of useful aspects of clinical condition, pathology, or other information which may be relevant to long term prognosis. Again, this may be done on either a protein or gene level, with the use of genes being preferred. Single or multiple genes may be useful in various combinations. As above, prostate cancer probes may be attached to biochips for the detection and quantification of prostate cancer sequences in a tissue or patient. The assays proceed as outlined above for diagnosis. PCR method may provide more sensitive and accurate quantification.

Assays for therapeutic compounds

In a preferred embodiment members of the proteins, nucleic acids, and antibodies as described herein are used in drug screening assays. The prostate cancer proteins, antibodies, nucleic acids, modified proteins, and cells containing prostate cancer sequences are used in drug screening assays or by evaluating the effect of drug candidates on a “gene expression profile” or expression profile of polypeptides. In a preferred embodiment, the expression profiles are used, preferably in conjunction with high throughput screening techniques to allow monitoring for expression profile genes after treatment with a candidate agent (e.g., Zlokarnik, et al. (1998) Science 279:84-88; Heid (1996) Genome Res. 6:986-94).

In a preferred embodiment, the prostate cancer proteins, antibodies, nucleic acids, modified proteins, and cells containing the native or modified prostate cancer proteins are used in screening assays. That is, the present invention provides novel methods for screening for compositions which modulate the prostate cancer phenotype or an identified physiological function of a prostate cancer protein. As above, this can be done on an individual gene level or by evaluating the effect of drug candidates on a “gene expression profile”. In a preferred embodiment, the expression profiles are used, preferably in conjunction with high throughput screening techniques to allow monitoring for expression profile genes after treatment with a candidate agent, see Zlokarnik, supra.

Having identified the differentially expressed genes herein, a variety of assays may be executed. In a preferred embodiment, assays may be run on an individual gene or protein level. That is, having identified a particular gene as up regulated in prostate cancer, test

compounds can be screened for the ability to modulate gene expression or for binding to the prostate cancer protein. "Modulation" thus includes both an increase and a decrease in gene expression. The preferred amount of modulation will depend on the original change of the gene expression in normal versus tissue undergoing prostate cancer, with changes of at least 5 10%, preferably 50%, more preferably 100-300%, and in some embodiments 300-1000% or greater. Thus, if a gene exhibits a 4-fold increase in prostate cancer tissue compared to normal tissue, a decrease of about four-fold is often desired; similarly, a 10-fold decrease in prostate cancer tissue compared to normal tissue often provides a target value of a 10-fold increase in expression to be induced by the test compound.

10 The amount of gene expression may be monitored using nucleic acid probes and the quantification of gene expression levels, or, alternatively, the gene product itself can be monitored, e.g., through the use of antibodies to the prostate cancer protein and standard immunoassays. Proteomics and separation techniques may also allow quantification of expression.

15 In a preferred embodiment, gene expression or protein monitoring of a number of entities, i.e., an expression profile, is monitored simultaneously. Such profiles will typically involve a plurality of those entities described herein.

In this embodiment, the prostate cancer nucleic acid probes are attached to biochips as outlined herein for the detection and quantification of prostate cancer sequences in a 20 particular cell. Alternatively, PCR may be used. Thus, a series, e.g., of microtiter plate, may be used with dispensed primers in desired wells. A PCR reaction can then be performed and analyzed for each well.

Expression monitoring can be performed to identify compounds that modify the expression of one or more prostate cancer-associated sequences, e.g., a polynucleotide 25 sequence set out in Tables 1A-4. Generally, in a preferred embodiment, a test modulator is added to the cells prior to analysis. Moreover, screens are also provided to identify agents that modulate prostate cancer, modulate prostate cancer proteins, bind to a prostate cancer protein, or interfere with the binding of a prostate cancer protein and an antibody or other binding partner.

30 The term "test compound" or "drug candidate" or "modulator" or grammatical equivalents as used herein describes a molecule, e.g., protein, oligopeptide, small organic molecule, polysaccharide, polynucleotide, etc., to be tested for the capacity to directly or

indirectly alter the prostate cancer phenotype or the expression of a prostate cancer sequence, e.g., a nucleic acid or protein sequence. In preferred embodiments, modulators alter expression profiles, or expression profile nucleic acids or proteins provided herein. In one embodiment, the modulator suppresses a prostate cancer phenotype, e.g., to a normal or non-malignant tissue fingerprint. In another embodiment, a modulator induced a prostate cancer phenotype. Generally, a plurality of assay mixtures are run in parallel with different agent concentrations to obtain a differential response to the various concentrations. Typically, one of these concentrations serves as a negative control, i.e., at zero concentration or below the level of detection.

Drug candidates encompass numerous chemical classes, though typically they are organic molecules, preferably small organic compounds having a molecular weight of more than 100 and less than about 2,500 daltons. Preferred small molecules are less than 2000, or less than 1500, or less than 1000, or less than 500 D. Candidate agents comprise functional groups necessary for structural interaction with proteins, particularly hydrogen bonding, and typically include at least an amine, carbonyl, hydroxyl or carboxyl group, preferably at least two of the functional chemical groups. The candidate agents often comprise cyclical carbon or heterocyclic structures and/or aromatic or polyaromatic structures substituted with one or more of the above functional groups. Candidate agents are also found among biomolecules including peptides, saccharides, fatty acids, steroids, purines, pyrimidines, derivatives, structural analogs, or combinations thereof. Particularly preferred are peptides.

In one aspect, a modulator will neutralize the effect of a prostate cancer protein. By “neutralize” is meant that activity of a protein is inhibited or blocked and the consequent effect on the cell.

In certain embodiments, combinatorial libraries of potential modulators will be screened for an ability to bind to a prostate cancer polypeptide or to modulate activity. Conventionally, new chemical entities with useful properties are generated by identifying a chemical compound (called a “lead compound”) with some desirable property or activity, e.g., inhibiting activity, creating variants of the lead compound, and evaluating the property and activity of those variant compounds. Often, high throughput screening (HTS) methods are employed for such an analysis.

In one preferred embodiment, high throughput screening methods involve providing a library containing a large number of potential therapeutic compounds (candidate

compounds). Such “combinatorial chemical libraries” are then screened in one or more assays to identify those library members (particular chemical species or subclasses) that display a desired characteristic activity. The compounds thus identified can serve as conventional “lead compounds” or can themselves be used as potential or actual therapeutics.

5 A combinatorial chemical library is a collection of diverse chemical compounds generated by either chemical synthesis or biological synthesis by combining a number of chemical “building blocks” such as reagents. For example, a linear combinatorial chemical library, such as a polypeptide (e.g., mutein) library, is formed by combining a set of chemical building blocks called amino acids in most every possible way for a given compound length
10 (i.e., the number of amino acids in a polypeptide compound). Millions of chemical compounds can be synthesized through such combinatorial mixing of chemical building blocks. Gallop, et al. (1994) J. Med. Chem. 37:1233-1251.

Preparation and screening of combinatorial chemical libraries is well known to those of skill in the art. Such combinatorial chemical libraries include, but are not limited to,
15 peptide libraries (see, e.g., U.S. Patent No. 5,010,175, Furka (1991) Pept. Prot. Res. 37:487-493, Houghton, et al. (1991) Nature, 354:84-88), peptoids (PCT Publication No WO 91/19735), encoded peptides (PCT Publication WO 93/20242), random bio-oligomers (PCT Publication WO 92/00091), benzodiazepines (U.S. Pat. No. 5,288,514), diversomers such as hydantoins, benzodiazepines and dipeptides (Hobbs, et al. (1993) Proc. Nat. Acad. Sci. USA
20 90:6909-6913), vinylogous polypeptides (Hagihara, et al. (1992) J. Amer. Chem. Soc. 114:6568-xxx), nonpeptidal peptidomimetics with a Beta-D-Glucose scaffolding (Hirschmann, et al. (1992) J. Amer. Chem. Soc. 114:9217-9218), analogous organic syntheses of small compound libraries (Chen, et al. (1994) J. Amer. Chem. Soc. 116:2661-xxx), oligocarbamates (Cho, et al. (1993) Science 261:1303-1305), and/or peptidyl
25 phosphonates (Campbell, et al. (1994) J. Org. Chem. 59:658-xxx). See, generally, Gordon, et al. (1994) J. Med. Chem. 37:1385-1401), nucleic acid libraries (see, e.g., Stratagene, Corp.), peptide nucleic acid libraries (see, e.g., U.S. Patent 5,539,083), antibody libraries (see, e.g., Vaughn, et al. (1996) Nature Biotechnology 14:309-314, and PCT/US96/10287), carbohydrate libraries (see, e.g., Liang, et al. (1996) Science 274:1520-1522, and U.S. Patent
30 No. 5,593,853), and small organic molecule libraries (see, e.g., benzodiazepines, Baum (1993) C&EN, Jan 18, page 33; isoprenoids, U.S. Patent No. 5,569,588; thiazolidinones and metathiazanones, U.S. Patent No. 5,549,974; pyrrolidines, U.S. Patent Nos. 5,525,735 and

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5,519,134; morpholino compounds, U.S. Patent No. 5,506,337; benzodiazepines, U.S. Patent No. 5,288,514; and the like).

Devices for the preparation of combinatorial libraries are commercially available (see, e.g., 357 MPS, 390 MPS, Advanced Chem Tech, Louisville KY, Symphony, Rainin, Woburn, MA, 433A Applied Biosystems, Foster City, CA, 9050 Plus, Millipore, Bedford, MA).

A number of well known robotic systems have also been developed for solution phase chemistries. These systems include automated workstations like the automated synthesis apparatus developed by Takeda Chemical Industries, LTD. (Osaka, Japan) and many robotic systems utilizing robotic arms (Zymate II, Zymark Corporation, Hopkinton, Mass.; Orca, Hewlett-Packard, Palo Alto, Calif.), which mimic the manual synthetic operations performed by a chemist. Many of the above devices are suitable for use with the present invention. The nature and implementation of modifications to these devices (if any) so that they can operate as discussed herein will be apparent to persons skilled in the relevant art. In addition, numerous combinatorial libraries are themselves commercially available (see, e.g., ComGenex, Princeton, N.J., Asinex, Moscow, Ru, Tripos, Inc., St. Louis, MO, ChemStar, Ltd, Moscow, RU, 3D Pharmaceuticals, Exton, PA, Martek Biosciences, Columbia, MD, etc.).

The assays to identify modulators are amenable to high throughput screening. Preferred assays thus detect enhancement or inhibition of prostate cancer gene transcription, inhibition or enhancement of polypeptide expression, and inhibition or enhancement of polypeptide activity.

High throughput assays for the presence, absence, quantification, or other properties of particular nucleic acids or protein products are well known to those of skill in the art. Similarly, binding assays and reporter gene assays are similarly well known. Thus, e.g., U.S. Patent No. 5,559,410 discloses high throughput screening methods for proteins, U.S. Patent No. 5,585,639 discloses high throughput screening methods for nucleic acid binding (i.e., in arrays), while U.S. Patent Nos. 5,576,220 and 5,541,061 disclose high throughput methods of screening for ligand/antibody binding.

In addition, high throughput screening systems are commercially available (see, e.g., Zymark Corp., Hopkinton, MA; Air Technical Industries, Mentor, OH; Beckman Instruments, Inc. Fullerton, CA; Precision Systems, Inc., Natick, MA, etc.). These systems

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typically automate entire procedures, including sample and reagent pipetting, liquid dispensing, timed incubations, and final readings of the microplate in detector(s) appropriate for the assay. These configurable systems provide high throughput and rapid start up as well as a high degree of flexibility and customization. The manufacturers of such systems provide
5 detailed protocols for various high throughput systems. Thus, e.g., Zymark Corp. provides technical bulletins describing screening systems for detecting the modulation of gene transcription, ligand binding, and the like.

In one embodiment, modulators are proteins, often naturally occurring proteins or fragments of naturally occurring proteins. Thus, e.g., cellular extracts containing proteins, or
10 random or directed digests of proteinaceous cellular extracts, may be used. In this way libraries of proteins may be made for screening in the methods of the invention. Particularly preferred in this embodiment are libraries of bacterial, fungal, viral, and mammalian proteins, with the latter being preferred, and human proteins being especially preferred. Particularly useful test compound will be directed to the class of proteins to which the target belongs, e.g.,
15 substrates for enzymes or ligands and receptors.

In a preferred embodiment, modulators are peptides of from about 5 to about 30 amino acids, with from about 5 to about 20 amino acids being preferred, and from about 7 to about 15 being particularly preferred. The peptides may be digests of naturally occurring proteins as is outlined above, random peptides, or "biased" random peptides. By
20 "randomized" or grammatical equivalents herein is meant that each nucleic acid and peptide consists of essentially random nucleotides and amino acids, respectively. Since generally these random peptides (or nucleic acids, discussed below) are chemically synthesized, they may typically incorporate any nucleotide or amino acid at any position. The synthetic process can be designed to generate randomized proteins or nucleic acids, to allow the
25 formation of all or most of the possible combinations over the length of the sequence, thus forming a library of randomized candidate bioactive proteinaceous agents.

In one embodiment, the library is fully randomized, with no sequence preferences or constants at any position. In a preferred embodiment, the library is biased. That is, some positions within the sequence are either held constant, or are selected from a limited number
30 of possibilities. For example, in a preferred embodiment, the nucleotides or amino acid residues are randomized within a defined class, e.g., of hydrophobic amino acids, hydrophilic residues, sterically biased (either small or large) residues, towards the creation of nucleic acid

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binding domains, the creation of cysteines, for cross-linking, prolines for SH-3 domains, serines, threonines, tyrosines, or histidines for phosphorylation sites, etc., or to purines, etc.

Modulators of prostate cancer can also be nucleic acids, as defined above.

As described above generally for proteins, nucleic acid modulating agents may be
5 naturally occurring nucleic acids, random nucleic acids, or “biased” random nucleic acids. For example, digests of prokaryotic or eukaryotic genomes may be used as is outlined above for proteins.

In a preferred embodiment, the candidate compounds are organic chemical moieties, a wide variety of which are available in the literature.

10 After the candidate agent has been added and the cells allowed to incubate for some period of time, the sample containing a target sequence to be analyzed is added to the biochip. If required, the target sequence is prepared using known techniques. For example, the sample may be treated to lyse the cells, using known lysis buffers, electroporation, etc., with purification and/or amplification such as PCR performed as appropriate. For example,
15 an in vitro transcription with labels covalently attached to the nucleotides is performed. Generally, the nucleic acids are labeled with biotin-FITC or PE, or with cy3 or cy5.

In a preferred embodiment, the target sequence is labeled with, e.g., a fluorescent, a chemiluminescent, a chemical, or a radioactive signal, to provide a means of detecting the target sequence’s specific binding to a probe. The label also can be an enzyme, such as,
20 alkaline phosphatase or horseradish peroxidase, which when provided with an appropriate substrate produces a product that can be detected. Alternatively, the label can be a labeled compound or small molecule, such as an enzyme inhibitor, that binds but is not catalyzed or altered by the enzyme. The label also can be a moiety or compound, such as, an epitope tag or biotin which specifically binds to streptavidin. For the example of biotin, the streptavidin
25 is labeled as described above, thereby, providing a detectable signal for the bound target sequence. Unbound labeled streptavidin is typically removed prior to analysis.

As will be appreciated by those in the art, these assays can be direct hybridization assays or can comprise “sandwich assays”, which include the use of multiple probes, as is generally outlined in U.S. Patent Nos. 5,681,702, 5,597,909, 5,545,730, 5,594,117,
30 5,591,584, 5,571,670, 5,580,731, 5,571,670, 5,591,584, 5,624,802, 5,635,352, 5,594,118, 5,359,100, 5,124,246, and 5,681,697, each of which is hereby incorporated by reference. In this embodiment, in general, the target nucleic acid is prepared as outlined above, and then

added to the biochip comprising a plurality of nucleic acid probes, under conditions that allow the formation of a hybridization complex.

A variety of hybridization conditions may be used in the present invention, including high, moderate, and low stringency conditions as outlined above. The assays are generally
5 run under stringency conditions which allows formation of the label probe hybridization complex only in the presence of target. Stringency can be controlled by altering a step parameter that is a thermodynamic variable, including, but not limited to, temperature, formamide concentration, salt concentration, chaotropic salt concentration pH, organic solvent concentration, etc.

10 These parameters may also be used to control non-specific binding, as is generally outlined in U.S. Patent No. 5,681,697. Thus it may be desirable to perform certain steps at higher stringency conditions to reduce non-specific binding.

The reactions outlined herein may be accomplished in a variety of ways. Components of the reaction may be added simultaneously, or sequentially, in different orders, with
15 preferred embodiments outlined below. In addition, the reaction may include a variety of other reagents. These include salts, buffers, neutral proteins, e.g., albumin, detergents, etc., which may be used to facilitate optimal hybridization and detection, and/or reduce non-specific or background interactions. Reagents that otherwise improve the efficiency of the assay, such as protease inhibitors, nuclease inhibitors, anti-microbial agents, etc., may also be
20 used as appropriate, depending on the sample preparation methods and purity of the target.

The assay data are analyzed to determine the expression levels, and changes in expression levels as between states, of individual genes, forming a gene expression profile.

Screens are performed to identify modulators of the prostate cancer or related phenotype. In one embodiment, screening is performed to identify modulators that can
25 induce or suppress a particular expression profile, thus preferably generating the associated phenotype. In another embodiment, e.g., for diagnostic applications, having identified differentially expressed genes important in a particular state, screens can be performed to identify modulators that alter expression of individual genes. In an another embodiment, screening is performed to identify modulators that alter a biological function of the
30 expression product of a differentially expressed gene. Again, having identified the importance of a gene in a particular state, screens are performed to identify agents that bind and/or modulate the biological activity of the gene product.

In addition screens can be done for genes that are induced in response to a candidate agent. After identifying a modulator based upon its ability to suppress a prostate cancer expression pattern leading to a normal expression pattern, or to modulate a single prostate cancer gene expression profile so as to mimic the expression of the gene from normal tissue, a screen as described above can be performed to identify genes that are specifically modulated in response to the agent. Comparing expression profiles between normal tissue and agent treated prostate cancer tissue reveals genes that are not expressed in normal tissue or prostate cancer tissue, but are expressed in agent treated tissue. These agent-specific sequences can be identified and used by methods described herein for prostate cancer genes or proteins. In particular these sequences and the proteins they encode find use in marking or identifying agent treated cells. In addition, antibodies can be raised against the agent induced proteins and used to target novel therapeutics to the treated prostate cancer tissue sample.

Thus, in one embodiment, a test compound is administered to a population of prostate cancer cells, that have an associated prostate cancer expression profile. By “administration” or “contacting” herein is meant that the candidate agent is added to the cells in such a manner as to allow the agent to act upon the cell, whether by uptake and intracellular action, or by action at the cell surface. In some embodiments, nucleic acid encoding a proteinaceous candidate agent (e.g., a peptide) may be put into a viral construct such as an adenoviral or retroviral construct, and added to the cell, such that expression of the peptide agent is accomplished, e.g., PCT US97/01019. Regulatable gene therapy systems can also be used.

Once the test compound has been administered to the cells, the cells can be washed if desired and are allowed to incubate under preferably physiological conditions for some period of time. The cells are then harvested and a new gene expression profile is generated, as outlined herein.

Thus, e.g., prostate cancer or non-malignant tissue may be screened for agents that modulate, e.g., induce or suppress the prostate cancer or related phenotype. A change in at least one gene, preferably many, of the expression profile indicates that the agent has an effect on prostate cancer activity. By defining such a signature for the prostate cancer phenotype, screens for new drugs that alter the phenotype can be devised. With this approach, the drug target need not be known and need not be represented in the original expression screening platform, nor does the level of transcript for the target protein need to change.

In a preferred embodiment, as outlined above, screens may be done on individual genes and gene products (proteins). That is, having identified a particular differentially expressed gene as important in a particular state, screening of modulators of either the expression of the gene or the gene product itself can be done. The gene products of differentially expressed genes are sometimes referred to herein as “prostate cancer proteins” or a “prostate cancer modulatory protein”. The prostate cancer modulatory protein may be a fragment, or alternatively, be the full length protein to the fragment encoded by the nucleic acids of the Tables 1A-4. Preferably, the prostate cancer modulatory protein is a fragment. In a preferred embodiment, the prostate cancer amino acid sequence which is used to determine sequence identity or similarity is encoded by a nucleic acid of Tables 1A-4. In another embodiment, the sequences are naturally occurring allelic variants of a protein encoded by a nucleic acid of Tables 1A-4. In another embodiment, the sequences are sequence variants as further described herein.

Preferably, the prostate cancer modulatory protein is a fragment of approximately 14 to 24 amino acids long. More preferably the fragment is a soluble fragment. Preferably, the fragment includes a non-transmembrane region. In a preferred embodiment, the fragment has an N-terminal Cys to aid in solubility. In one embodiment, the C-terminus of the fragment is kept as a free acid and the N-terminus is a free amine to aid in coupling, i.e., to cysteine.

In one embodiment the prostate cancer proteins are conjugated to an immunogenic agent as discussed herein. In one embodiment the prostate cancer protein is conjugated to BSA.

Measurements of prostate cancer polypeptide activity, or of prostate cancer or the prostate cancer phenotype can be performed using a variety of assays. For example, the effects of the test compounds upon the function of the prostate cancer polypeptides can be measured by examining parameters described above. A suitable physiological change that affects activity can be used to assess the influence of a test compound on the polypeptides of this invention. When the functional consequences are determined using intact cells or animals, one can also measure a variety of effects such as, in the case of prostate cancer associated with tumors, tumor growth, tumor metastasis, neovascularization, hormone release, transcriptional changes to both known and uncharacterized genetic markers (e.g., northern blots), changes in cell metabolism such as cell growth or pH changes, and changes

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in intracellular second messengers such as cGMP. In the assays of the invention, a mammalian prostate cancer polypeptide is typically used, e.g., mouse, preferably human.

Assays to identify compounds with modulating activity can be performed in vitro. For example, a prostate cancer polypeptide is first contacted with a potential modulator and incubated for a suitable amount of time, e.g., from 0.5 to 48 hours. In one embodiment, the prostate cancer polypeptide levels are determined in vitro by measuring the level of protein or mRNA. The level of protein is measured using immunoassays such as western blotting, ELISA, and the like with an antibody that selectively binds to the prostate cancer polypeptide or a fragment thereof. For measurement of mRNA, amplification, e.g., using PCR, LCR, or hybridization assays, e.g., northern hybridization, RNase protection, dot blotting, are preferred. The level of protein or mRNA is detected using directly or indirectly labeled detection agents, e.g., fluorescently or radioactively labeled nucleic acids, radioactively or enzymatically labeled antibodies, and the like, as described herein.

Alternatively, a reporter gene system can be devised using the prostate cancer protein promoter operably linked to a reporter gene such as luciferase, green fluorescent protein, CAT, or β -gal. The reporter construct is typically transfected into a cell. After treatment with a potential modulator, the amount of reporter gene transcription, translation, or activity is measured according to standard techniques known to those of skill in the art.

In a preferred embodiment, as outlined above, screens may be done on individual genes and gene products (proteins). That is, having identified a particular differentially expressed gene as important in a particular state, screening of modulators of the expression of the gene or the gene product itself can be done. The gene products of differentially expressed genes are sometimes referred to herein as "prostate cancer proteins." The prostate cancer protein may be a fragment, or alternatively, be the full length protein corresponding to a fragment shown herein.

In one embodiment, screening for modulators of expression of specific genes is performed. Typically, the expression of only one or a few genes are evaluated. In another embodiment, screens are designed to first find compounds that bind to differentially expressed proteins. These compounds are then evaluated for the ability to modulate differentially expressed activity. Moreover, once initial candidate compounds are identified, variants can be further screened to better evaluate structure activity relationships.

In a preferred embodiment, binding assays are done. In general, purified or isolated gene product is used; that is, the gene products of one or more differentially expressed nucleic acids are made. For example, antibodies are generated to the protein gene products, and standard immunoassays are run to determine the amount of protein present.

5 Alternatively, cells comprising the prostate cancer proteins can be used in the assays.

Thus, in a preferred embodiment, the methods comprise combining a prostate cancer protein and a candidate compound, and determining the binding of the compound to the prostate cancer protein. Preferred embodiments utilize the human prostate cancer protein, although other mammalian proteins may also be used, e.g., for the development of animal
10 models of human disease. In some embodiments, as outlined herein, variant or derivative prostate cancer proteins may be used.

Generally, in a preferred embodiment of the methods herein, the prostate cancer protein or the candidate agent is non-diffusably bound to an insoluble support having isolated sample receiving areas (e.g., a microtiter plate, an array, etc.). The insoluble supports may be
15 made of a composition to which the compositions can be bound, is readily separated from soluble material, and is otherwise compatible with the overall method of screening. The surface of such supports may be solid or porous and of a convenient shape. Examples of suitable insoluble supports include microtiter plates, arrays, membranes, and beads. These are typically made of glass, plastic (e.g., polystyrene), polysaccharides, nylon or
20 nitrocellulose, teflon™, etc. Microtiter plates and arrays are especially convenient because a large number of assays can be carried out simultaneously, using small amounts of reagents and samples. The particular manner of binding of the composition should be compatible with the reagents and overall methods of the invention, maintain the activity of the composition, and be nondiffusable. Preferred methods of binding include the use of antibodies (which do
25 not sterically block either the ligand binding site or activation sequence when the protein is bound to the support), direct binding to "sticky" or ionic supports, chemical crosslinking, the synthesis of the protein or agent on the surface, etc. Following binding of the protein or agent, excess unbound material is removed by washing. The sample receiving areas may then be blocked through incubation with bovine serum albumin (BSA), casein, or other
30 innocuous protein or other moiety.

In a preferred embodiment, the prostate cancer protein is bound to the support, and a test compound is added to the assay. Alternatively, the candidate agent is bound to the

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support and the prostate cancer protein is added. Novel binding agents include specific antibodies, non-natural binding agents identified in screens of chemical libraries, peptide analogs, etc. Of particular interest are screening assays for agents that have a low toxicity for human cells. A wide variety of assays may be used for this purpose, including labeled in
5 vitro protein-protein binding assays, electrophoretic mobility shift assays, immunoassays for protein binding, functional assays (phosphorylation assays, etc.) and the like.

The determination of the binding of the test modulating compound to the prostate cancer protein may be done in a number of ways. In a preferred embodiment, the compound is labeled, and binding determined directly, e.g., by attaching all or a portion of the prostate
10 cancer protein to a solid support, adding a labeled candidate agent (e.g., a fluorescent label), washing off excess reagent, and determining whether the label is present on the solid support. Various blocking and washing steps may be utilized as appropriate.

In some embodiments, only one of the components is labeled, e.g., the proteins (or proteinaceous candidate compounds) can be labeled. Alternatively, more than one
15 component can be labeled with different labels, e.g., ^{125}I for the proteins and a fluorophor for the compound. Proximity reagents, e.g., quenching or energy transfer reagents are also useful.

In one embodiment, the binding of the test compound is determined by competitive binding assay. The competitor is a binding moiety known to bind to the target molecule (i.e.,
20 a prostate cancer protein), such as an antibody, peptide, binding partner, ligand, etc. Under certain circumstances, there may be competitive binding between the compound and the binding moiety, with the binding moiety displacing the compound. In one embodiment, the test compound is labeled. Either the compound, or the competitor, or both, is added first to the protein for a time sufficient to allow binding, if present. Incubations may be performed at
25 a temperature which facilitates optimal activity, typically between 4 and 40° C. Incubation periods are typically optimized, e.g., to facilitate rapid high throughput screening. Typically between 0.1 and 1 hour will be sufficient. Excess reagent is generally removed or washed away. The second component is then added, and the presence or absence of the labeled component is followed, to indicate binding.

30 In a preferred embodiment, the competitor is added first, followed by the test compound. Displacement of the competitor is an indication that the test compound is binding to the prostate cancer protein and thus is capable of binding to, and potentially modulating,

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the activity of the prostate cancer protein. In this embodiment, either component can be labeled. Thus, e.g., if the competitor is labeled, the presence of label in the wash solution indicates displacement by the agent. Alternatively, if the test compound is labeled, the presence of the label on the support indicates displacement.

5 In an alternative embodiment, the test compound is added first, with incubation and washing, followed by the competitor. The absence of binding by the competitor may indicate that the test compound is bound to the prostate cancer protein with a higher affinity. Thus, if the test compound is labeled, the presence of the label on the support, coupled with a lack of competitor binding, may indicate that the test compound is capable of binding to the prostate
10 cancer protein.

 In a preferred embodiment, the methods comprise differential screening to identify agents that are capable of modulating the activity of the prostate cancer proteins. In this embodiment, the methods comprise combining a prostate cancer protein and a competitor in a first sample. A second sample comprises a test compound, a prostate cancer protein, and a
15 competitor. The binding of the competitor is determined for both samples, and a change, or difference in binding between the two samples indicates the presence of an agent capable of binding to the prostate cancer protein and potentially modulating its activity. That is, if the binding of the competitor is different in the second sample relative to the first sample, the agent is capable of binding to the prostate cancer protein.

20 Alternatively, differential screening is used to identify drug candidates that bind to the native prostate cancer protein, but cannot bind to modified prostate cancer proteins. The structure of the prostate cancer protein may be modeled, and used in rational drug design to synthesize agents that interact with that site. Drug candidates that affect the activity of a prostate cancer protein are also identified by screening drugs for the ability to either enhance
25 or reduce the activity of the protein.

 Positive controls and negative controls may be used in the assays. Preferably control and test samples are performed in at least triplicate to obtain statistically significant results. Incubation of samples is for a time sufficient for the binding of the agent to the protein. Following incubation, samples are washed free of non-specifically bound material and the
30 amount of bound, generally labeled agent determined. For example, where a radiolabel is employed, the samples may be counted in a scintillation counter to determine the amount of bound compound.

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A variety of other reagents may be included in the screening assays. These include reagents like salts, neutral proteins, e.g., albumin, detergents, etc., which may be used to facilitate optimal protein-protein binding and/or reduce non-specific or background interactions. Also reagents that otherwise improve the efficiency of the assay, such as
5 protease inhibitors, nuclease inhibitors, anti-microbial agents, etc., may be used. The mixture of components may be added in an order that provides for the requisite binding.

In a preferred embodiment, the invention provides methods for screening for a compound capable of modulating the activity of a prostate cancer protein. The methods comprise adding a test compound, as defined above, to a cell comprising prostate cancer
10 proteins. Preferred cell types include almost any cell. The cells contain a recombinant nucleic acid that encodes a prostate cancer protein. In a preferred embodiment, a library of candidate agents are tested on a plurality of cells.

In one aspect, the assays are evaluated in the presence or absence or previous or subsequent exposure of physiological signals, e.g., hormones, antibodies, peptides, antigens,
15 cytokines, growth factors, action potentials, pharmacological agents including chemotherapeutics, radiation, carcinogenics, or other cells (e.g., cell-cell contacts). In another example, the determinations are determined at different stages of the cell cycle process.

In this way, compounds that modulate prostate cancer agents are identified.
20 Compounds with pharmacological activity are able to enhance or interfere with the activity of the prostate cancer protein. Once identified, similar structures are evaluated to identify critical structural feature of the compound.

In one embodiment, a method of inhibiting prostate cancer cell division is provided. The method comprises administration of a prostate cancer inhibitor. In another embodiment,
25 a method of inhibiting prostate cancer or other prostate proliferative condition is provided. The method comprises administration of a prostate cancer inhibitor. In a further embodiment, methods of treating cells or individuals with prostate cancer are provided. The method comprises administration of a prostate cancer inhibitor.

In one embodiment, a prostate cancer inhibitor is an antibody as discussed above. In
30 another embodiment, the prostate cancer inhibitor is an antisense molecule.

A variety of cell growth, proliferation, and metastasis assays are known to those of skill in the art, as described below.

Soft agar growth or colony formation in suspension

Normal cells require a solid substrate to attach and grow. When the cells are transformed, they lose this phenotype and grow detached from the substrate. For example, transformed cells can grow in stirred suspension culture or suspended in semi-solid media, such as semi-solid or soft agar. The transformed cells, when transfected with tumor suppressor genes, regenerate normal phenotype and require a solid substrate to attach and grow. Soft agar growth or colony formation in suspension assays can be used to identify modulators of prostate cancer sequences, which when expressed in host cells, inhibit abnormal cellular proliferation and transformation. A therapeutic compound would reduce or eliminate the host cells' ability to grow in stirred suspension culture or suspended in semi-solid media, such as semi-solid or soft.

Techniques for soft agar growth or colony formation in suspension assays are described in Freshney (1994) Culture of Animal Cells a Manual of Basic Technique 3d ed. Wiley-Liss, herein incorporated by reference. See also, the methods section of Garkavtsev, et al. (1996), supra, herein incorporated by reference.

Contact inhibition and density limitation of growth

Normal cells typically grow in a flat and organized pattern in a petri dish until they touch other cells. When the cells touch one another, they are contact inhibited and stop growing. When cells are transformed, however, the cells are not contact inhibited and continue to grow to high densities in disorganized foci. Thus, the transformed cells grow to a higher saturation density than normal cells. This can be detected morphologically by the formation of a disoriented monolayer of cells or rounded cells in foci within the regular pattern of normal surrounding cells. Alternatively, labeling index with (^3H)-thymidine at saturation density can be used to measure density limitation of growth. See Freshney (1994), supra. The transformed cells, when transfected with tumor suppressor genes, regenerate a normal phenotype and become contact inhibited and would grow to a lower density.

In this assay, labeling index with (^3H)-thymidine at saturation density is a preferred method of measuring density limitation of growth. Transformed host cells are transfected with a prostate cancer-associated sequence and are grown for 24 hours at saturation density in non-limiting medium conditions. The percentage of cells labeling with (^3H)-thymidine is determined autoradiographically. See, Freshney (1994), supra.

Growth factor or serum dependence

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Transformed cells have a lower serum dependence than their normal counterparts (see, e.g., Temin (1966) J. Natl. Cancer Inst. 37:167-175; Eagle, et al. (1970) J. Exp. Med. 131:836-879); Freshney, supra. This is in part due to release of various growth factors by the transformed cells. Growth factor or serum dependence of transformed host cells can be

5 compared with that of control.

Tumor specific markers levels

Tumor cells release an increased amount of certain factors (hereinafter "tumor specific markers") than their normal counterparts. For example, plasminogen activator (PA) is released from human glioma at a higher level than from normal brain cells (see, e.g.,

10 Gullino, "Angiogenesis, tumor vascularization, and potential interference with tumor growth" pp. 178-184 in Mihich (ed. 1985) Biological Responses in Cancer Plenum. Similarly, Tumor angiogenesis factor (TAF) is released at a higher level in tumor cells than their normal counterparts. See, e.g., Folkman (1992) Angiogenesis and Cancer, Sem. Cancer Biol.

Various techniques which measure the release of these factors are described in

15 Freshney (1994), supra. Also, see, Unkless, et al. (1974) J. Biol. Chem. 249:4295-4305; Strickland and Beers (1976) J. Biol. Chem. 251:5694-5702; Whur, et al. (1980) Br. J. Cancer 42:305-312; Gullino, "Angiogenesis, tumor vascularization, and potential interference with tumor growth" pp. 178-184 in Mihich (ed. 1985) Biological Responses in Cancer Plenum; and Freshney (1985) Anticancer Res. 5:111-130.

Invasiveness into Matrigel

The degree of invasiveness into Matrigel or some other extracellular matrix constituent can be used as an assay to identify compounds that modulate prostate cancer-associated sequences. Tumor cells exhibit a good correlation between malignancy and invasiveness of cells into Matrigel or some other extracellular matrix constituent. In this

25 assay, tumorigenic cells are typically used as host cells. Expression of a tumor suppressor gene in these host cells would decrease invasiveness of the host cells.

Techniques described in Freshney (1994), supra, can be used. Briefly, the level of invasion of host cells can be measured by using filters coated with Matrigel or some other extracellular matrix constituent. Penetration into the gel, or through to the distal side of the

30 filter, is rated as invasiveness, and rated histologically by number of cells and distance moved, or by prelabeling the cells with ^{125}I and counting the radioactivity on the distal side of the filter or bottom of the dish. See, e.g., Freshney (1984), supra.

Tumor growth in vivo

Effects of prostate cancer-associated sequences on cell growth can be tested in transgenic or immune-suppressed mice. Knock-out transgenic mice can be made, in which the prostate cancer gene is disrupted or in which a prostate cancer gene is inserted. Knock-out transgenic mice can be made by insertion of a marker gene or other heterologous gene into the endogenous prostate cancer gene site in the mouse genome via homologous recombination. Such mice can also be made by substituting the endogenous prostate cancer gene with a mutated version of the prostate cancer gene, or by mutating the endogenous prostate cancer gene, e.g., by exposure to carcinogens.

A DNA construct is introduced into the nuclei of embryonic stem cells. Cells containing the newly engineered genetic lesion are injected into a host mouse embryo, which is re-implanted into a recipient female. Some of these embryos develop into chimeric mice that possess germ cells partially derived from the mutant cell line. Therefore, by breeding the chimeric mice it is possible to obtain a new line of mice containing the introduced genetic lesion (see, e.g., Capecchi, et al. (1989) Science 244:1288-1292). Chimeric targeted mice can be derived according to Hogan, et al. (1988) Manipulating the Mouse Embryo: A Laboratory Manual CSH Press; and Robertson (ed. 1987) Teratocarcinomas and Embryonic Stem Cells: A Practical Approach IRL Press, Washington, D.C.

Alternatively, various immune-suppressed or immune-deficient host animals can be used. For example, genetically athymic “nude” mouse (see, e.g., Giovanella, et al. (1974) J. Natl. Cancer Inst. 52:921-930), a SCID mouse, a thymectomized mouse, or an irradiated mouse (see, e.g., Bradley, et al. (1978) Br. J. Cancer 38:263-272; Selby, et al. (1980) Br. J. Cancer 41:52-61) can be used as a host. Transplantable tumor cells (typically about 10^6 cells) injected into isogenic hosts will produce invasive tumors in a high proportions of cases, while normal cells of similar origin will not. In hosts which developed invasive tumors, cells expressing a prostate cancer-associated sequences are injected subcutaneously. After a suitable length of time, preferably 4-8 weeks, tumor growth is measured (e.g., by volume or by its two largest dimensions) and compared to the control. Tumors that have statistically significant reduction (using, e.g., Student’s T test) are said to have inhibited growth.

Polynucleotide modulators of prostate cancer

Antisense and RNAi Polynucleotides

In certain embodiments, the activity of a prostate cancer-associated protein is down-regulated, or entirely inhibited, by the use of antisense polynucleotide, i.e., a nucleic acid complementary to, and which can preferably hybridize specifically to, a coding mRNA nucleic acid sequence, e.g., a prostate cancer protein mRNA, or a subsequence thereof.

5 Binding of the antisense polynucleotide to the mRNA reduces the translation and/or stability of the mRNA.

In the context of this invention, antisense polynucleotides can comprise naturally-occurring nucleotides, or synthetic species formed from naturally-occurring subunits or their close homologs. Antisense polynucleotides may also have altered sugar moieties or inter-
10 sugar linkages. Exemplary among these are the phosphorothioate and other sulfur containing species which are known for use in the art. Analogs are comprehended by this invention so long as they function effectively to hybridize with the prostate cancer protein mRNA. See, e.g., Isis Pharmaceuticals, Carlsbad, CA; Sequitor, Inc., Natick, MA.

Such antisense polynucleotides can readily be synthesized using recombinant means,
15 or can be synthesized in vitro. Equipment for such synthesis is sold by several vendors, including Applied Biosystems. The preparation of other oligonucleotides such as phosphorothioates and alkylated derivatives is also well known to those of skill in the art.

Antisense molecules as used herein include antisense or sense oligonucleotides. Sense oligonucleotides can, e.g., be employed to block transcription by binding to the anti-
20 sense strand. The antisense and sense oligonucleotide comprise a single-stranded nucleic acid sequence (either RNA or DNA) capable of binding to target mRNA (sense) or DNA (antisense) sequences for prostate cancer molecules. A preferred antisense molecule is for a prostate cancer sequences in Tables 1A-4, or for a ligand or activator thereof. Antisense or sense oligonucleotides, according to the present invention, comprise a fragment generally at
25 least about 14 nucleotides, preferably from about 14 to 30 nucleotides. The ability to derive an antisense or a sense oligonucleotide, based upon a cDNA sequence encoding a given protein is described in, e.g., Stein and Cohen (1988) Cancer Res. 48:2659-2668; and van der Krol, et al. (1988) BioTechniques 6:958-976.

RNA interference is a mechanism to suppress gene expression in a sequence specific
30 manner. See, e.g., Brumelkamp, et al. (2002) Scienceexpress (21March2002); Sharp (1999) Genes Dev. 13:139-141; and Cathew (2001) Curr. Op. Cell Biol. 13:244-248. In mammalian cells, short, e.g., 21 nt, double stranded small interfering RNAs (siRNA) have been shown to

be effective at inducing an RNAi response. See, e.g., Elbashir, et al. (2001) Nature 411:494-498. The mechanism may be used to downregulate expression levels of identified genes, e.g., treatment of or validation of relevance to disease.

5 Ribozymes

In addition to antisense polynucleotides, ribozymes can be used to target and inhibit transcription of prostate cancer-associated nucleotide sequences. A ribozyme is an RNA molecule that catalytically cleaves other RNA molecules. Different kinds of ribozymes have been described, including group I ribozymes, hammerhead ribozymes, hairpin ribozymes,
10 RNase P, and axhead ribozymes (see, e.g., Castanotto, et al. (1994) Adv. in Pharmacology 25: 289-317 for a general review of the properties of different ribozymes).

The general features of hairpin ribozymes are described, e.g., in Hampel, et al. (1990) Nucl. Acids Res. 18:299-304; European Patent Publication No. 0 360 257; U.S. Patent No. 5,254,678. Methods of preparing are well known to those of skill in the art. See, e.g., WO
15 94/26877; Ojwang, et al. (1993) Proc. Natl. Acad. Sci. USA 90:6340-6344; Yamada, et al. (1994) Human Gene Therapy 1:39-45; Leavitt, et al. (1995) Proc. Natl. Acad. Sci. USA 92:699-703; Leavitt, et al. (1994) Human Gene Therapy 5:1151-120; and Yamada, et al. (1994) Virology 205:121-126.

Polynucleotide modulators of prostate cancer may be introduced into a cell containing
20 the target nucleotide sequence by formation of a conjugate with a ligand binding molecule, as described in WO 91/04753. Suitable ligand binding molecules include, but are not limited to, cell surface receptors, growth factors, other cytokines, or other ligands that bind to cell surface receptors. Preferably, conjugation of the ligand binding molecule does not substantially interfere with the ability of the ligand binding molecule to bind to its
25 corresponding molecule or receptor, or block entry of the sense or antisense oligonucleotide or its conjugated version into the cell. Alternatively, a polynucleotide modulator of prostate cancer may be introduced into a cell containing the target nucleic acid sequence, e.g., by formation of an polynucleotide-lipid complex, as described in WO 90/10448. It is understood that the use of antisense molecules or knock out and knock in models may also be
30 used in screening assays as discussed above, in addition to methods of treatment.

Thus, in one embodiment, methods of modulating prostate disorders, e.g., cancer in cells or organisms, are provided. In one embodiment, the methods comprise administering to

a patient, e.g., to a cell within the patient, an anti-prostate cancer antibody that reduces or eliminates the biological activity of an endogenous prostate cancer protein. Alternatively, the methods comprise administering to a cell or organism a recombinant nucleic acid encoding a prostate cancer protein. This may be accomplished in many ways. In a preferred
5 embodiment, e.g., when the prostate cancer sequence is down-regulated in prostate cancer, such state may be reversed by increasing the amount of prostate cancer gene product in the cell. This can be accomplished, e.g., by overexpressing the endogenous prostate cancer gene or administering a gene encoding the prostate cancer sequence, using known gene-therapy techniques, e.g.. In a preferred embodiment, the gene therapy techniques include the
10 incorporation of the exogenous gene using enhanced homologous recombination (EHR), e.g., as described in PCT/US93/03868, hereby incorporated by reference in its entirety.

Alternatively, e.g., when the prostate cancer sequence is up-regulated in prostate cancer, the activity of the endogenous prostate cancer gene is decreased, e.g., by the administration of a prostate cancer antisense nucleic acid.

15 In one embodiment, the prostate cancer proteins of the present invention may be used to generate polyclonal and monoclonal antibodies to prostate cancer proteins. Similarly, the prostate cancer proteins can be coupled, using standard technology, to affinity chromatography columns. These columns may then be used to purify prostate cancer antibodies useful for production, diagnostic, or therapeutic purposes. In a preferred
20 embodiment, the antibodies are generated to epitopes unique to a prostate cancer protein; that is, the antibodies show little or no cross-reactivity to other proteins. The prostate cancer antibodies may be coupled to standard affinity chromatography columns and used to purify prostate cancer proteins. The antibodies may also be used as blocking polypeptides, as outlined above, since they will specifically bind to the prostate cancer protein.

25

Methods of identifying variant prostate cancer-associated sequences

Without being bound by theory, expression of various prostate cancer sequences is correlated with prostate cancer or other prostate disorders. Accordingly, disorders based on mutant or variant prostate cancer genes may be determined. In one embodiment, the
30 invention provides methods for identifying cells containing variant prostate cancer genes, e.g., determining all or part of the sequence of at least one endogenous prostate cancer genes in a cell. This may be accomplished using many sequencing techniques. In a preferred

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embodiment, the invention provides methods of identifying the prostate cancer genotype of an individual, e.g., determining all or part of the sequence of at least one prostate cancer gene of the individual. This is generally done in at least one tissue of the individual, and may include the evaluation of a number of tissues or different samples of the same tissue. The
5 method may include comparing the sequence of the sequenced prostate cancer gene to a known prostate cancer gene, e.g., a wild-type gene.

The sequence of all or part of the prostate cancer gene can then be compared to the sequence of a known prostate cancer gene to determine if differences exist. This can be done using many known homology programs, such as Bestfit, etc. In a preferred embodiment, the
10 presence of a difference in the sequence between the prostate cancer gene of the patient and the known prostate cancer gene correlates with a disease state or a propensity for a disease state, as outlined herein.

In a preferred embodiment, the prostate cancer genes are used as probes to determine the number of copies of the prostate cancer gene in the genome.

15 In another preferred embodiment, the prostate cancer genes are used as probes to determine the chromosomal localization of the prostate cancer genes. Information such as chromosomal localization finds use in providing a diagnosis or prognosis in particular when chromosomal abnormalities such as translocations, and the like are identified in the prostate cancer gene locus.

20

Administration of pharmaceutical and vaccine compositions

In one embodiment, a therapeutically effective dose of a prostate cancer protein or modulator thereof, is administered to a patient. By "therapeutically effective dose" herein is meant a dose that produces effects for which it is administered. The exact dose will depend
25 on the purpose of the treatment, and will be ascertainable by one skilled in the art using known techniques (e.g., Ansel, et al. (1992) Pharmaceutical Dosage Forms and Drug Delivery; Lieberman (1993) Pharmaceutical Dosage Forms (vols. 1-3, Dekker, ISBN 0824770846, 082476918X, 0824712692, 0824716981; Lloyd (1999) The Art, Science and Technology of Pharmaceutical Compounding Amer. Pharma. Assn.; and Pickar (1999)
30 Dosage Calculations Thomson). Adjustments for prostate cancer degradation, systemic versus localized delivery, and rate of new protease synthesis, as well as the age, body weight, general health, sex, diet, time of administration, drug interaction, and the severity of the

condition may be necessary, and will be ascertainable with routine experimentation by those skilled in the art. U.S. Patent Application N. 09/687,576 further discloses the use of compositions and methods of diagnosis and treatment in prostate cancer is hereby expressly incorporated by reference.

5 A “patient” for the purposes of the present invention includes both humans and other animals, particularly mammals. Thus the methods are applicable to both human therapy and veterinary applications. In the preferred embodiment the patient is a mammal, preferably a primate, and in the most preferred embodiment the patient is human. The patient typically will suffer from a prostate proliferative disorder, e.g., malignant or non-malignant, and may
10 include cancer of other related conditions or disorders.

 The administration of the prostate cancer proteins and modulators thereof of the present invention can be done in a variety of ways as discussed above, including, but not limited to, orally, subcutaneously, intravenously, intranasally, transdermally, intraperitoneally, intramuscularly, intrapulmonary, vaginally, rectally, or intraocularly. In
15 some instances, e.g., in the treatment of wounds and inflammation, the prostate cancer proteins and modulators may be directly applied as a solution or spray, or via catheter.

 The pharmaceutical compositions of the present invention comprise a prostate cancer protein in a form suitable for administration to a patient. In the preferred embodiment, the pharmaceutical compositions are in a water soluble form, such as being present as
20 pharmaceutically acceptable salts, which is meant to include both acid and base addition salts. “Pharmaceutically acceptable acid addition salt” refers to those salts that retain the biological effectiveness of the free bases and that are not biologically or otherwise undesirable, formed with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid and the like, and organic acids such as acetic acid, propionic acid, glycolic acid, pyruvic acid, oxalic acid, maleic acid, malonic acid, succinic
25 acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, salicylic acid, and the like. “Pharmaceutically acceptable base addition salts” include those derived from inorganic bases such as sodium, potassium, lithium, ammonium, calcium, magnesium, iron, zinc, copper,
30 manganese, aluminum salts, and the like. Particularly preferred are the ammonium, potassium, sodium, calcium, and magnesium salts. Salts derived from pharmaceutically acceptable organic non-toxic bases include salts of primary, secondary, and tertiary amines,

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substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins, such as isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, and ethanolamine.

The pharmaceutical compositions may also include one or more of the following:

5 carrier proteins such as serum albumin; buffers; fillers such as microcrystalline cellulose, lactose, corn and other starches; binding agents; sweeteners and other flavoring agents; coloring agents; and polyethylene glycol.

The pharmaceutical compositions can be administered in a variety of unit dosage forms depending upon the method of administration. For example, unit dosage forms

10 suitable for oral administration include, but are not limited to, powder, tablets, pills, capsules and lozenges. It is recognized that prostate cancer protein modulators (e.g., antibodies, antisense constructs, ribozymes, small organic molecules, etc.) when administered orally, should be protected from digestion. This is typically accomplished either by complexing the molecule(s) with a composition to render it resistant to acidic and enzymatic hydrolysis, or by

15 packaging the molecule(s) in an appropriately resistant carrier, such as a liposome or a protection barrier. Means of protecting agents from digestion are well known in the art.

The compositions for administration will commonly comprise a prostate cancer protein modulator dissolved in a pharmaceutically acceptable carrier, preferably an aqueous carrier. A variety of aqueous carriers can be used, e.g., buffered saline and the like. These

20 solutions are typically sterile and generally free of undesirable matter. These compositions may be sterilized by conventional, well known sterilization techniques. The compositions may contain pharmaceutically acceptable auxiliary substances as required to approximate physiological conditions such as pH adjusting and buffering agents, toxicity adjusting agents and the like, e.g., sodium acetate, sodium chloride, potassium chloride, calcium chloride,

25 sodium lactate, and the like. The concentration of active agent in these formulations can vary widely, and will be selected primarily based on fluid volumes, viscosities, body weight, and the like in accordance with the particular mode of administration selected and the patient's needs (e.g., (1980) Remington's Pharmaceutical Science (15th ed.); and Hardman, et al. (eds. 2001) Goodman & Gilman: The Pharmacological Basis of Therapeutics McGraw-Hill.

30 Thus, a typical pharmaceutical composition for intravenous administration would be about 0.1 to 10 mg per patient per day. Dosages from 0.1 up to about 100 mg per patient per day may be used, particularly when the drug is administered to a secluded site and not into

the blood stream, such as into a body cavity or into a lumen of an organ. Substantially higher dosages are possible in topical administration. Actual methods for preparing parenterally administrable compositions will be known or apparent to those skilled in the art, e.g., Remington's Pharmaceutical Science and Goodman and Gilman: The Pharmacological Basis of Therapeutics, supra.

The compositions containing modulators of prostate cancer proteins can be administered for therapeutic or prophylactic treatments. In therapeutic applications, compositions are administered to a patient suffering from a disease (e.g., a cancer) in an amount sufficient to cure or at least partially retard or arrest the disease and its complications.

An amount adequate to accomplish this is defined as a "therapeutically effective dose." Amounts effective for this use will depend upon the severity of the disease and the general state of the patient's health. Single or multiple administrations of the compositions may be administered depending on the dosage and frequency as required and tolerated by the patient. The composition should provide a sufficient quantity of the agents of this invention to effectively treat the patient. An amount of modulator that is capable of preventing or slowing the development of cancer in a mammal is referred to as a "prophylactically effective dose." The particular dose required for a prophylactic treatment will depend upon the medical condition and history of the mammal, the particular cancer being prevented, as well as other factors such as age, weight, gender, administration route, efficiency, etc. Such prophylactic treatments may be used, e.g., in a mammal who has previously had cancer to prevent a recurrence of the cancer, or in a mammal who is suspected of having a significant likelihood of developing cancer, e.g., based partly on gene expression profiles.

It will be appreciated that the present prostate cancer protein-modulating compounds can be administered alone or in combination with additional prostate cancer modulating compounds or with other therapeutic agent, e.g., other anti-cancer agents or treatments.

In numerous embodiments, one or more nucleic acids, e.g., polynucleotides comprising nucleic acid sequences set forth in Tables 1A-4 such as antisense polynucleotides, silencing RNA, or ribozymes, will be introduced into cells, in vitro or in vivo. The present invention provides methods, reagents, vectors, and cells useful for expression of prostate cancer-associated polypeptides and nucleic acids using in vitro (cell-free), ex vivo or in vivo (cell or organism-based) recombinant expression systems.

The particular procedure used to introduce the nucleic acids into a host cell for expression of a protein or nucleic acid is application specific. Many procedures for introducing foreign nucleotide sequences into host cells may be used. These include the use of calcium phosphate transfection, spheroplasts, electroporation, liposomes, microinjection, plasma vectors, viral vectors, and many other well known methods for introducing cloned genomic DNA, cDNA, synthetic DNA, or other foreign genetic material into a host cell (see, e.g., Berger and Kimmel (1987) Guide to Molecular Cloning Techniques from Methods in Enzymology (vol. 152) Academic Press; Ausubel, et al., (eds. supplemented through 1999) Current Protocols Lippincott; and Sambrook, et al. (1989) Molecular Cloning: A Laboratory Manual (2d ed., Vol. 1-3) CSH Press.

In a preferred embodiment, prostate cancer proteins and modulators are administered as therapeutic agents, and can be formulated as outlined above. Similarly, prostate cancer genes (including both the full-length sequence, partial sequences, or regulatory sequences of the prostate cancer coding regions) can be administered in a gene therapy application. These prostate cancer genes can include antisense applications, either as gene therapy (i.e., for incorporation into the genome) or as antisense compositions, as will be appreciated by those in the art.

Prostate cancer polypeptides and polynucleotides can also be administered as vaccine compositions to stimulate HTL, CTL, and antibody responses.. Such vaccine compositions can include, e.g., lipidated peptides (see, e.g., Vitiello, et al. (1995) J. Clin. Invest. 95:341-349), peptide compositions encapsulated in poly(DL-lactide-co-glycolide) ("PLG") microspheres (see, e.g., Eldridge, et al. (1991) Molec. Immunol. 28:287-294; Alonso, et al. (1994) Vaccine 12:299-306; Jones, et al. (1995) Vaccine 13:675-681), peptide compositions contained in immune stimulating complexes (ISCOMS) (see, e.g., Takahashi, et al. (1990) Nature 344:873-875; Hu, et al. (1998) Clin Exp Immunol. 113:235-243), multiple antigen peptide systems (MAPs) (see, e.g., Tam (1988) Proc. Natl. Acad. Sci. USA 85:5409-5413; Tam (1996) J. Immunol. Methods 196:17-32), peptides formulated as multivalent peptides; peptides for use in ballistic delivery systems, typically crystallized peptides, viral delivery vectors (Perkus, et al., p. 379, in Kaufmann (ed. 1996) Concepts in vaccine development de Gruyter; Chakrabarti, et al. (1986) Nature 320:535-537; Hu, et al. (1986) Nature 320:537-540; Kieny, et al. (1986) AIDS Bio/Technology 4:790-xxx; Top, et al. (1971) J. Infect. Dis. 124:148-154; Chanda, et al. (1990) Virology 175:535-547), particles of viral or synthetic

origin (see, e.g., Kofler, et al. (1996) J. Immunol. Methods 192:25-35; Eldridge, et al. (1993) Sem. Hematol. 30:16-24; Falo, et al. (1995) Nature Med. 7:649-653), adjuvants (Warren, et al. (1986) Annu. Rev. Immunol. 4:369-388; Gupta, et al. (1993) Vaccine 11:293-306), liposomes (Reddy, et al. (1992) J. Immunol. 148:1585-1589; Rock (1996) Immunol. Today 17:131-137), or, naked or particle absorbed cDNA (Ulmer, et al. (1993) Science 259:1745-1749; Robinson, et al. (1993) Vaccine 11:957-960; Shiver, et al., p. 423, in Kaufmann (ed. 1996) Concepts in Vaccine Development de Gruyter; Cease and Berzofsky (1994) Annu. Rev. Immunol. 12:923-989; and Eldridge, et al. (1993) Sem. Hematol. 30:16-24). Toxin-targeted delivery technologies, also known as receptor mediated targeting, such as those of Avant Immunotherapeutics, Inc. (Needham, Massachusetts) may also be used.

Vaccine compositions often include adjuvants. Many adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, Bortadella pertussis or Mycobacterium tuberculosis derived proteins. Certain adjuvants are commercially available as, e.g., Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A, and quil A. Cytokines, such as GM-CSF, interleukin-2, -7, -12, and other like growth factors, may also be used as adjuvants.

Vaccines can be administered as nucleic acid compositions wherein DNA or RNA encoding one or more of the polypeptides, or a fragment thereof, is administered to a patient. This approach is described, for instance, in Wolff, et al. (1990) Science 247:1465-1468 as well as U.S. Patent Nos. 5,580,859; 5,589,466; 5,804,566; 5,739,118; 5,736,524; 5,679,647; WO 98/04720; and in more detail below. Examples of DNA-based delivery technologies include "naked DNA", facilitated (bupivacaine, polymers, peptide-mediated) delivery, cationic lipid complexes, and particle-mediated ("gene gun") or pressure-mediated delivery (see, e.g., U.S. Patent No. 5,922,687).

For therapeutic or prophylactic immunization purposes, the peptides of the invention can be expressed by viral or bacterial vectors. Examples of expression vectors include

attenuated viral hosts, such as vaccinia or fowlpox. This approach involves the use of vaccinia virus, e.g., as a vector to express nucleotide sequences that encode prostate cancer polypeptides or polypeptide fragments. Upon introduction into a host, the recombinant vaccinia virus expresses the immunogenic peptide, and thereby elicits an immune response.

5 Vaccinia vectors and methods useful in immunization protocols are described in, e.g., U.S. Patent No. 4,722,848. Another vector is BCG (Bacille Calmette Guerin). BCG vectors are described in Stover, et al. (1991) Nature 351:456-460. A wide variety of other vectors useful for therapeutic administration or immunization, e.g., adeno and adeno-associated virus vectors, retroviral vectors, Salmonella typhi vectors, detoxified anthrax toxin vectors, and the
10 like, will be apparent to those skilled in the art from the description herein (see, e.g., Shata, et al. (2000) Mol. Med. Today 6:66-71; Shedlock, et al. (2000) J. Leuk. Biol. 68:793-806; Hipp, et al. (2000) In Vivo 14:571-85).

Methods for the use of genes as DNA vaccines are well known, and include placing a prostate cancer gene or portion of a prostate cancer gene under the control of a regulatable
15 promoter or a tissue-specific promoter for expression in a prostate cancer patient. The prostate cancer gene used for DNA vaccines can encode full-length prostate cancer proteins, but more preferably encodes portions of the prostate cancer proteins including peptides derived from the prostate cancer protein. In one embodiment, a patient is immunized with a DNA vaccine comprising a plurality of nucleotide sequences derived from a prostate cancer
20 gene. For example, prostate cancer-associated genes or sequence encoding subfragments of a prostate cancer protein are introduced into expression vectors and tested for their immunogenicity in the context of Class I MHC and an ability to generate cytotoxic T cell responses. This procedure may provide for production of cytotoxic T lymphocyte responses against cells which present antigen, including intracellular epitopes.

25 In a preferred embodiment, the DNA vaccines include a gene encoding an adjuvant molecule with the DNA vaccine. Such adjuvant molecules include cytokines that increase the immunogenic response to the prostate cancer polypeptide encoded by the DNA vaccine. Additional or alternative adjuvants are available.

In another preferred embodiment prostate cancer genes find use in generating animal
30 models of prostate cancer. When the prostate cancer gene identified is repressed or diminished in cancer tissue, gene therapy technology, e.g., wherein antisense RNA directed to the prostate cancer gene will also diminish or repress expression of the gene. Animal

models of prostate cancer find use in screening for modulators of a prostate cancer-associated sequence or modulators of prostate cancer. Similarly, transgenic animal technology including gene knockout technology, e.g., as a result of homologous recombination with an appropriate gene targeting vector, will result in the absence or increased expression of the prostate cancer protein. When desired, tissue-specific expression or knockout of the prostate cancer protein may be necessary.

It is also possible that the prostate cancer protein is overexpressed in prostate cancer. As such, transgenic animals can be generated that overexpress the prostate cancer protein. Depending on the desired expression level, promoters of various strengths can be employed to express the transgene. Also, the number of copies of the integrated transgene can be determined and compared for a determination of the expression level of the transgene. Animals generated by such methods find use as animal models of prostate cancer and are additionally useful in screening for modulators to treat prostate cancer.

Kits for Use in Diagnostic and/or Prognostic Applications

For use in diagnostic, research, and therapeutic applications suggested above, kits are also provided by the invention. In the diagnostic and research applications such kits may include one of the following: assay reagents, buffers, prostate cancer-specific nucleic acids or antibodies, hybridization probes and/or primers, antisense polynucleotides, silencing RNA, ribozymes, dominant negative prostate cancer polypeptides or polynucleotides, small molecules inhibitors of prostate cancer-associated sequences, etc. A therapeutic product may include sterile saline or another pharmaceutically acceptable emulsion and suspension base.

In addition, the kits may include instructional materials containing instructions (i.e., protocols) for the practice of the methods of this invention. While the instructional materials typically comprise written or printed materials they are not limited to such. A medium capable of storing such instructions and communicating them to an end user is contemplated by this invention. Such media include, but are not limited to electronic storage media (e.g., magnetic discs, tapes, cartridges, chips), optical media (e.g., CD ROM), and the like. Such media may include addresses to internet sites that provide such instructional materials.

The present invention also provides for kits for screening for modulators of prostate cancer-associated sequences. Such kits can be prepared from readily available materials and reagents. For example, such kits can comprise one or more of the following materials: a

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prostate cancer-associated polypeptide or polynucleotide, reaction tubes, and instructions for testing prostate cancer-associated activity. Optionally, the kit contains biologically active prostate cancer protein. A wide variety of kits and components can be prepared according to the present invention, depending upon the intended user of the kit and the particular needs of

5 the user. Diagnosis would typically involve evaluation of a plurality of genes or products. The genes will be selected based on correlations with important parameters in disease which may be identified in historical or outcome data.

EXAMPLES

Example 1: Gene Chip Analyses of Expression Profiles

Molecular profiles of various normal and cancerous tissues were determined and analyzed using gene chips. RNA was isolated and gene chip analysis was performed as described (Glynn, et al. (2000) *Nature* 403:672-676; Zhao, et al. (2000) *Genes Dev.* 14:981-993).

EXAMPLE 2: Identification of androgen dependent/independent genes

To identify gene expression changes during the transition from androgen-dependent to androgen-independent prostate cancer, oligonucleotide microarrays ("K" chips or Affymetrix Eos Hu03) were interrogated with cRNAs derived from the human CWR22 prostate cancer xenograft model propagated in nude mice (Pretlow, et al. (1993) *J. Natl. Cancer Inst.* 85:394-398). The CWR22 xenograft is androgen-dependent when grown in male Nude mice. Androgen-independent sub-lines can be derived by first establishing androgen-dependent tumors in male mice. The mice are then castrated to remove the primary source of growth stimulus (androgen), resulting in tumor regression. Within 3-10 months molecular events prompt the tumors to relapse and start growing as androgen-independent tumors. See, e.g., Nagabhushan, et al. (1996) *Cancer Res.* 56:3042-3046; Amler, et al. (2000) *Cancer Res.* 60:6134-6141; and Bubendorf, et al. (1999) *J. Natl. Cancer Inst.* 91:1758-1764.

Using the CWR22 xenograft model, tumors were grown subcutaneously in male nude mice. Tumors were harvested at different times after castration. The time points post-castration included (in days): 0, 1, 3, 4, 5, 10, 30, 40, 50, 51, 52, 59, 60, 61, 70, 79, 80, 82, 120, and 125. Analyses also included established androgen-independent xenografts. Castration resulted in tumor regression. At day 120 and thereafter, the tumors relapsed and started growing in the absence of androgen.

cRNAs were generated by in vitro transcription assays (IVTs) from the different samples and were hybridized to the oligonucleotide microarrays (Affymetrix Eos Hu03). Hybridization was measured by the average fluorescence intensity (AI), which is directly proportional to the expression level of the gene.

Two types of analyses were applied to the results:

Analysis A:

The samples were divided into different time groups which included the following time points post castration (in days): 1-5, 10, 30-40, 50-82, 120-125. To identify changes in gene expression, the following calculations were made:

1. The median (or mean, in case there were only 2 samples in a group) was calculated
5 for each group.
2. The medians (or means) for each group was compared to one-another.
3. Genes were selected that exhibited a minimum 2 fold difference in the median (or mean) between any of the groups.
4. The change in gene expression over time was analyzed for each selected gene to look
10 for specific pattern changes.

Only genes with an interesting expression pattern during the androgen-ablation time course were selected as potential new therapeutic targets and/or diagnostic markers. Among the 70,000 gene clusters present on Hu01 and Hu02, we identified 820 gene clusters with the desired expression patterns. These expression patterns can be broadly defined into the
15 following categories:

1. Genes that are expressed early in the time course, then drop off in expression, and then express again with emergence of androgen-independence (hi-lo-hi pattern in Table 1A).
2. Genes that are expressed early in the time course, then drop off in expression, and do not express again with emergence of androgen-independence (hi-lo-lo pattern in Table 1A).
- 20 3. Genes that are not expressed early in the time course, but express only with emergence of androgen-independence (lo-lo-hi pattern in Table 1A).
4. Genes that are not expressed early in the time course, but then express as androgen is withdrawn and continue to express with emergence of androgen-independence (lo-hi-hi pattern in Table 1A).
- 25 5. Genes that are not expressed early in the time course, but then express as androgen is withdrawn and drop off again with emergence of androgen-independence (lo-hi-lo pattern in Table 1A).

Group 1 is characterized by cell-cycle regulating genes, such as those encoding cyclin B1, p21/WAF1, CDC18-homolog, cyclin A2, cyclin D1, and possible growth factors
30 such as hAG2 (anterior gradient 2 homolog) among others. This indicates that interruption of growth factor and/or cell cycle pathways prevents the emergence of androgen-independent disease, making group 1 genes good targets for treating advanced prostate cancer.

Group 2 represents genes that are androgen-dependent, and do not re-express due to the lack of androgen signal in the androgen-independent phenotype. This group includes genes encoding proteins such as Fibronectin 1, which has been previously shown to be down-regulated with androgen-withdrawal (Amler, et al. (2000) Cancer Res. 60:6134-6141).

5 Group 3 represents genes that are up-regulated by signals that induce the androgen-independent phenotype. This group includes genes encoding stanniocalcin 2, c-fos proto-oncogene product, vascular endothelial growth factor, the cell surface protein transmembrane 4 superfamily member 1 and adrenomedullin among others. Adrenomedullin has recently been shown to act as an autocrine growth factor for the androgen-independent prostate cancer
10 cell line DU145 (Rocchi, et al. (2001) Cancer Res. 61:1196-1206), indicating that its up-regulation is critical for supporting an androgen-independent phenotype. Blocking adrenomedullin function, and/or other genes in this group, prevents the growth of androgen-independent tumor cells.

 Group 4 represents genes that are androgen-repressed and are only expressed in the
15 absence of androgen. This group includes genes encoding the protein tyrosine phosphatase interacting protein liprin-alpha 2, the CD24 antigen, and the catalytic subunit for phosphatidylinositol 4-kinase amongst others. Patients that are treated for advanced prostate cancer by hormone-ablation may have in their bodies cells that have survived hormone-ablation and are likely to up-regulate genes that belong to Group 4. Therefore, Group 4 gene
20 products are particularly good therapeutic targets for treating patients undergoing hormone-ablation therapy.

 Group 5 represents genes that are involved in regulating signals that induce an androgen-independent phenotype. This group includes genes encoding Rab2 (a Ras-like G protein), the Son of Sevenless homolog (a GTP/GDP exchange factor involved in activating
25 Ras-like proteins), and the p85 regulatory subunit for phosphoinositide-3-kinase (PI3-kinase). The PI3-kinase pathway has been implicated in providing a survival signal to the prostate cancer cell line LNCaP (Lin, et al. (1999) Cancer Res. 59:2891-2897). This indicates that ras-like signals and signals dependent on PI3-kinase are involved in inducing the androgen-independent phenotype. For that reason, Group 5 gene products are particularly good
30 therapeutic targets for treating patients undergoing hormone-ablation therapy.

Analysis B:

For the second analysis, the samples were divided into 4 time groups which included the following time points post castration (in days): 0-1, 3-5, 10-82, >120. To identify changes in gene expression, the following analysis was performed:

1. Genes were selected that exhibited a minimum of 100 AI units at the 90th percentile expression level of samples.
2. The group mean expression levels for each gene were calculated. The genes were further sub-selected to exhibit a minimum 3 fold difference between the group means.
3. An analysis of variance was then performed on selected genes. From the original 59,680 gene clusters present on the Hu03 gene chip, only about 1165 genes with a P value of < 0.01 were identified that also exhibited the above mentioned parameters.
4. A method was then employed for calculating the positive false discovery rate (pFDR), i.e., an estimate of the proportion of false-positives present in a set of findings (Storey and Tibshirani (2001) Technical Report, Department of Statistics, Stanford University, CA). This technique was developed explicitly for use with microarray data. The procedure involves randomly assigning the membership status of each sample to a group and re-performing the analysis of variance. In each simulation, the number of group members (6 for Group 1, 9 for group 2, 15 for group 3, and 4 for group 4) remained constant, but these designations were shuffled and assigned to each sample at random. The permutation was performed 1000 times, and for each simulation, the number of findings at $P < 0.01$ was noted. The number of false positives under null conditions, was then divided by the number of actual findings ($n=1165$ genes) to obtain an estimate of the proportion of false positive findings. After the application of a correction factor, the final estimate for the pFDR was about 1%. Thus, one can expect that approximately 12 of the 1165 findings are false positives.
5. The approximately 1165 genes were clustered by expression pattern to identify specific pattern changes. Only genes with an interesting expression pattern during the androgen-ablation time course were selected as potential new therapeutic targets and/or diagnostic markers. These expression patterns can be broadly defined into the following categories:
 1. Genes that are expressed early in the time course of androgen withdrawal, then drop off in expression, and then express again with emergence of androgen-independence (hi-lo-lo-hi pattern in Table 2A).

2. Genes that are expressed early in the time course, then drop off in expression immediately after androgen-withdrawal, and do not express again with emergence of androgen-independence (hi-lo-lo-lo pattern in Table 2A).

3. Genes that are expressed early in the time course, then drop off in expression after several
5 days of androgen withdrawal, and do not express again with emergence of androgen-independence (hi-hi-lo-lo pattern in Table 2A).

4. Genes that are not expressed early in the time course, but express only with emergence of androgen-independence (lo-lo-lo-hi pattern in Table 2A).

5. Genes that are not expressed early in the time course, but then express as androgen is
10 withdrawn and continue to express with emergence of androgen-independence (lo-lo-hi-hi pattern in Table 2A).

6. Genes that are not expressed early in the time course, but then express as androgen is withdrawn and drop off again with emergence of androgen-independence (lo-lo-hi-lo pattern in Table 2A).

15 Group 1 is characterized by cell-cycle regulating genes and cell growth promoting genes, such as those encoding cyclin B1 and CDC45 among others, growth factors/hormones such as hAG2 (anterior gradient 2 homolog), adrenomedullin, and stanniocalcin 2 among others, and growth factor receptors, such as the bone morphogenic protein receptor type 1B (BMP-R1B) and the endothelial differentiation lysophosphatidic acid G-protein-coupled
20 receptor 7 among others. Adrenomedullin has recently been shown to act as an autocrine growth factor for the androgen-independent prostate cancer cell line DU145 (Rocchi, et al. (2001) Cancer Res. 61:1196-1206), indicating that its up-regulation is critical for supporting an androgen-independent phenotype. This indicates that interruption of growth factor and/or cell cycle pathways prevents the emergence of androgen-independent disease, making group
25 1 genes good targets for treating both localized and advanced prostate cancer and related conditions.

 Group 2 represents genes that are androgen-dependent, and do not re-express due to the lack of androgen signal in the androgen-independent phenotype. This group includes genes encoding proteins such as the endothelial protein C receptor (EPCR) and the potassium
30 intermediate/small conductance calcium-activated channel (subfamily N, member 2). These genes represent targets for treating androgen-dependent prostate cancer and related conditions.

Group 3 also represents genes that are androgen-dependent, and do not re-express due to the lack of androgen signal in the androgen-independent phenotype. This group includes genes encoding proteins such as Fibronectin 1, which has been previously shown to be down-regulated with androgen-withdrawal (Amler, et al. (2000) Cancer Res. 60:6134-6141), and
5 genes encoding signaling proteins such as Rho GTPase activating protein 1. These genes represent targets for treating androgen-dependent prostate cancer and related conditions.

Group 4 represents genes that are up-regulated by signals that induce and maintain the androgen-independent phenotype. This group includes genes encoding potential growth promoting proteins such as chemokine-like factor (Unigene ID Hs.15159), colon cancer-associated protein Mic1, and the mitogen-activated protein kinase-activated protein kinase 2.
10 Blocking function of these proteins, and/or other genes in this group, prevents the growth of androgen-independent tumor cells and related conditions.

Group 5 represents genes that are androgen-repressed and are only expressed in the absence of androgen or that are induced by the absence of androgen. This group includes
15 genes encoding transcriptional regulators such as the androgen receptor, the DNA activated protein kinase (catalytic subunit), and nuclear factor related to kappa B binding protein (NFRKB), among others. Patients that are treated for advanced prostate cancer by hormone-ablation may have in their bodies cells that have survived hormone-ablation and are likely to up-regulate genes that belong to Group 5. Therefore, Group 5 gene products are particularly
20 good therapeutic targets for treating patients undergoing hormone-ablation therapy.

Group 6 represents genes that are involved in regulating signals that are induced during androgen withdrawal and that induce an androgen-independent phenotype. This group includes genes encoding signaling molecules such as phosphoinositide-3-kinase (class 2, alpha polypeptide), signal transducer and activator of transcription 2 (STAT2), phospholipase
25 A2 (group IIA) and the protein tyrosine phosphatase interacting protein liprin-alpha 2, cell surface receptors such as gamma-aminobutyric acid (GABA) A receptor epsilon subunit, G protein-coupled receptor 48, and immune function proteins such as the major histocompatibility complex class II DR alpha. The PI3-kinase pathway has been implicated in providing a survival signal to the prostate cancer cell line LNCaP (Lin, et al. (1999) Cancer
30 Res. 59:2891-2897). This indicates that ras-like signals and signals dependent on PI3-kinase are involved in inducing the androgen-independent phenotype. For that reason, Group 6 gene

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products are particularly good therapeutic targets for treating patients undergoing hormone-ablation therapy.

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TABLE 1A provides Accession numbers for genes, including expressed sequence tags, (incorporated in their entirety here and throughout the application where Accession numbers are provided). Genes with an interesting expression pattern during the androgen-ablation time course were selected as potential new therapeutic targets and/or diagnostic markers. 820 gene clusters were identified with desired expression patterns. These expression patterns can be broadly defined into the following categories:

1. Genes that are expressed early in the time course, then drop off in expression, and then express again with emergence of androgen-independence (hi-lo-hi pattern).
2. Genes that are expressed early in the time course, then drop off in expression, and do not express again with emergence of androgen-independence (hi-lo-lo pattern).
3. Genes that are not expressed early in the time course, but express only with emergence of androgen-independence (lo-lo-hi pattern).
4. Genes that are not expressed early in the time course, but then express as androgen is withdrawn and continue to express with emergence of androgen-independence (lo-hi-hi pattern).
5. Genes that are not expressed early in the time course, but then express as androgen is withdrawn and drop off again with emergence of androgen-independence (lo-hi-lo pattern).

Table 1B lists accession numbers for primekeys lacking a unigeneID in table 1A. For each probeset is listed a gene cluster number from which oligonucleotides were designed. Gene clusters were compiled using sequences derived from Genbank ESTs and mRNAs. These sequences were clustered based on sequence similarity using Clustering and Alignment Tools (DoubleTwist, Oakland California). Genbank accession numbers for sequences comprising each cluster are listed in the "Accession" column.

Table 1C lists genomic positioning for primekeys lacking unigene IDs and accession numbers in tables 1A. For each predicted exon is listed genomic sequence source used for prediction. Nucleotide locations of each predicted exon are also listed.

TABLE 1A

Pkey	ExAccon	UnigeneID	Unigene Title	pattern
102772	U83115	Hs.161002	absent in melanoma 1	hi-lo-hi
128610	N48373	Hs.10247	activated leucocyte cell adhesion molecu	hi-lo-hi
102276	N48373	Hs.10247	activated leucocyte cell adhesion molecu	hi-lo-hi
100654	A03758			hi-lo-hi
100655	A03758			hi-lo-hi
135400	X78592	Hs.99915	androgen receptor (dihydrotestosterone r	hi-lo-hi
331363	AW582256	"Hs.91011	anterior gradient 2 (Xenopus laevis) hom	hi-lo-hi
115764	AW582256	"Hs.91011	anterior gradient 2 (Xenopus laevis) hom	hi-lo-hi
120483	BE251623	Hs.1578	baculoviral IAP repeat-containing 5 (sur	hi-lo-hi
101505	AA307680	Hs.75692	asparagine synthetase	hi-lo-hi
127235	AW661857	Hs.98558	budding uninhibited by benzimidazoles 1	hi-lo-hi
128472	BE241880	"Hs.10029	cathepsin C	hi-lo-hi
102712	U77949	Hs.69563	CDC6 (cell division cycle 6, S. cerevisi	hi-lo-hi
314943	Y00272	Hs.184572	cell division cycle 2, G1 to S and G2 to	hi-lo-hi
102123	NM_001809	"Hs.1594	centromere protein A (17kD)	hi-lo-hi
326213			CH.17_hs_glj5867224	hi-lo-hi
327110			CH.21_hs_glj6117842	hi-lo-hi
339186			CH22_DA59H18.GENSCAN.72-13	hi-lo-hi
337755			CH22_EM:AC000097.GENSCAN.109-2	hi-lo-hi
337674			CH22_EM:AC000097.GENSCAN.67-4	hi-lo-hi
337675			CH22_EM:AC000097.GENSCAN.67-6	hi-lo-hi
333516			CH22_FGENES.173_1	hi-lo-hi
333517			CH22_FGENES.173_2	hi-lo-hi
333795			CH22_FGENES.275_1	hi-lo-hi
333796			CH22_FGENES.275_3	hi-lo-hi
333808			CH22_FGENES.279_2	hi-lo-hi
333809			CH22_FGENES.280_2	hi-lo-hi
332792			CH22_FGENES.3_2	hi-lo-hi
334101			CH22_FGENES.327_59	hi-lo-hi
334502			CH22_FGENES.397_18	hi-lo-hi
334616			CH22_FGENES.411_15	hi-lo-hi
334899			CH22_FGENES.452_13	hi-lo-hi
334900			CH22_FGENES.452_14	hi-lo-hi
334902			CH22_FGENES.452_16	hi-lo-hi
334905			CH22_FGENES.452_20	hi-lo-hi
334906			CH22_FGENES.452_21	hi-lo-hi
334951			CH22_FGENES.465_20	hi-lo-hi
335044			CH22_FGENES.480_1	hi-lo-hi
335753			CH22_FGENES.604_2	hi-lo-hi
335755			CH22_FGENES.604_4	hi-lo-hi
333135			CH22_FGENES.83_11	hi-lo-hi
333137			CH22_FGENES.83_13	hi-lo-hi
333138			CH22_FGENES.83_15	hi-lo-hi
333139			CH22_FGENES.83_16	hi-lo-hi
336721			CH22_FGENES.83-17	hi-lo-hi
105012	AF098158	Hs.9329	chromosome 20 open reading frame 1	hi-lo-hi
134470	X54942	Hs.83758	CDC28 protein kinase 2	hi-lo-hi
134750	L29073	Hs.1139	cold shock domain protein A	hi-lo-hi
125819	AA044840	"Hs.251871	CTP synthase	hi-lo-hi
102993	BE262998	Hs.85137	cyclin A2	hi-lo-hi
131185	BE280074	Hs.23960	cyclin B1	hi-lo-hi
106350	AK001404	"Hs.194698	cyclin B2	hi-lo-hi
103080	AU077231	"Hs.82932	cyclin D1 (PRAD1; parathyroid adenomas	hi-lo-hi
101216	AA284166	Hs.84113	cyclin-dependent kinase inhibitor 3 (CDK	hi-lo-hi
100689	AW247430	Hs.84152	cystathionine-beta-synthase	hi-lo-hi
130655	AI831962	Hs.17409	cysteine-rich protein 1 (intestinal)	hi-lo-hi
101473	M22976	Hs.83834	cytochrome b-5	hi-lo-hi
101468	BE538296	"Hs.181028	cytochrome c oxidase subunit Va	hi-lo-hi
103546	Z14244	"Hs.75752	cytochrome c oxidase subunit VIb	hi-lo-hi
100829	AA471098	Hs.278544	acetyl-Coenzyme A acetyltransferase 2 (a	hi-lo-hi
102469	AF058293	Hs.180015	D-dopachrome tautomerase	hi-lo-hi

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5	114292	AI815395	Hs.184641	fatty acid desaturase 2	hi-lo-hi
	100656	BE250162	"Hs.83765	dihydrofolate reductase	hi-lo-hi
	133799	W24087	Hs.76285	DKFZP564B167 protein	hi-lo-hi
	129113	BE543205	"Hs.288771	DKFZP568A0522 protein	hi-lo-hi
	332732	AF191019	Hs.8361	hypothetical protein, estradiol-induced	hi-lo-hi
10	108846	AL117452	"Hs.44155	DKFZP568G1517 protein	hi-lo-hi
	133903	XG3692	"Hs.77462	DNA (cytosine-5)-methyltransferase 1	hi-lo-hi
	320099	AW411307	Hs.114311	CDC45 (cell division cycle 45, S.cerevis	hi-lo-hi
	321960	AA723883	Hs.302448	hypothetical protein MGC10334	hi-lo-hi
	324988	AK001379	"Hs.121028	hypothetical protein FLJ10549	hi-lo-hi
15	303274	AK001468	Hs.62180	anillin (Drosophila Scraps homolog), act	hi-lo-hi
	301804	AK001468	Hs.62180	anillin (Drosophila Scraps homolog), act	hi-lo-hi
	300551	AW408800	Hs.104859	hypothetical protein DKFZp762E1312	hi-lo-hi
	304541	AA482561	Hs.169476	glyceraldehyde-3-phosphate dehydrogenase	hi-lo-hi
	304521	AA464716	"Hs.83765	gb:zx82c11.s1 Soares ovary tumor NbHOT H	hi-lo-hi
20	129075	BE250162	"Hs.83765	dihydrofolate reductase	hi-lo-hi
	111003	N52980	Hs.83765	dihydrofolate reductase	hi-lo-hi
	115536	AK001468	Hs.62180	anillin (Drosophila Scraps homolog), act	hi-lo-hi
	108857	AK001468	Hs.62180	anillin (Drosophila Scraps homolog), act	hi-lo-hi
	332397	AB027249	Hs.104741	PDZ-binding kinase; T-cell originated pr	hi-lo-hi
25	330714	AA263143	Hs.24596	RAD51-interacting protein	hi-lo-hi
	104636	R62252	Hs.106106	Homo sapiens cAMP-dependent protein kina	hi-lo-hi
	104986	AW088826	Hs.22971	ESTs	hi-lo-hi
	105076	AI598252	Hs.37810	ESTs	hi-lo-hi
	105312	BE613348	"Hs.23348	S-phase kinase-associated protein 2 (p45	hi-lo-hi
30	105388	AW575008	Hs.11355	thymopoietin	hi-lo-hi
	105953	BE410556	Hs.236555	hypothetical protein STRAIT11499	hi-lo-hi
	106286	AI765107	"Hs.274422	hypothetical protein FLJ20550	hi-lo-hi
	106889	U46258	Hs.18349	HSPC145 protein	hi-lo-hi
	109220	AW958181	Hs.189998	ESTs	hi-lo-hi
35	113158	AA328102	Hs.24641	cytoskeleton associated protein 2	hi-lo-hi
	114542	AW970128	"Hs.293380	ESTs	hi-lo-hi
	114986	AK000361	Hs.133260	hypothetical protein FLJ20354	hi-lo-hi
	115291	BE545072	"Hs.122579	hypothetical protein FLJ10461	hi-lo-hi
	115414	AA662240	Hs.283099	AF15q14 protein	hi-lo-hi
40	115471	AK001376	Hs.59346	hypothetical protein FLJ10514	hi-lo-hi
	115522	BE614387	Hs.47378	ESTs, Moderately similar to T50635 hypot	hi-lo-hi
	115652	BE093589	Hs.38178	hypothetical protein FLJ23468	hi-lo-hi
	116121	AK001330	Hs.48855	hypothetical protein FLJ10468	hi-lo-hi
	116130	AW183533	Hs.38178	hypothetical protein FLJ23468	hi-lo-hi
45	116448	BE268321	Hs.208912	hypothetical protein MGC861	hi-lo-hi
	116787	AW362955	Hs.15641	ESTs	hi-lo-hi
	118336	BE327311	Hs.47166	HT021	hi-lo-hi
	120649	AA687322	Hs.192843	leucine zipper protein FKSG14	hi-lo-hi
	121503	AA412049	Hs.290347	ESTs	hi-lo-hi
50	121748	BE536911	Hs.234545	Homo sapiens NUF2R mRNA, complete cds	hi-lo-hi
	122860	AA464414	"Hs.283532	gb:zx78g01.s1 Soares ovary tumor NbHOT H	hi-lo-hi
	123477	AF217515	"Hs.279918	uncharacterized bone marrow protein BM03	hi-lo-hi
	130338	AI375726	"Hs.183109	hypothetical protein	hi-lo-hi
	130680	BE567313	"Hs.303125	monocamine oxidase A	hi-lo-hi
55	131148	AW953575	"Hs.289092	p53-induced protein PIGPC1	hi-lo-hi
	131626	BE514605	"Hs.21446	Homo sapiens cDNA: FLJ22380 fis, clone H	hi-lo-hi
	131937	AI907735	Hs.35962	Homo sapiens mRNA for KIAA1716 protein,	hi-lo-hi
	131965	W79283	Hs.46677	ESTs	hi-lo-hi
	132371	AA235448	Hs.75277	PRO2000 protein	hi-lo-hi
60	133626	AW836130	Hs.122908	hypothetical protein FLJ13910	hi-lo-hi
	300942	AW301344	Hs.294088	Homo sapiens, clone IMAGE:3048353, mRNA,	hi-lo-hi
	300953	AA542845	Hs.70704	ESTs	hi-lo-hi
	302656	BE090580	Hs.270840	Homo sapiens, clone IMAGE:2823731, mRNA,	hi-lo-hi
	311928	T62216	Hs.126774	ESTs	hi-lo-hi
65	313637	AK000742	Hs.133294	L2DTL protein	hi-lo-hi
	313832	AW271106	Hs.121692	ESTs	hi-lo-hi
	316465	AW574774	Hs.181181	ESTs	hi-lo-hi
	317202	AA894880	Hs.117176	ESTs	hi-lo-hi
	320771	R74441	Hs.193465	poly(A)-binding protein, nuclear 1	hi-lo-hi
70	321636	AI820961	Hs.221197	ESTs	hi-lo-hi
	330867	AW978991	Hs.159420	ESTs	hi-lo-hi
	331442	H77381	Hs.286049	phosphoserine aminotransferase	hi-lo-hi
	106654	AW075485	Hs.301539	hypothetical protein MGC2633	hi-lo-hi
	106590	AI350260	Hs.237164	ESTs, Highly similar to LDHH_HUMAN L-LA	hi-lo-hi
75	128460	T16206	Hs.103291	neuritin	hi-lo-hi
	114394	T34462	Hs.271252	ESTs	hi-lo-hi
	315936	AW069807	Hs.91521	hypothetical protein	hi-lo-hi
	108886	AW248434	Hs.109706	hematological and neurological expressed	hi-lo-hi
	129241	AI878857	Hs.19322	ESTs, Weakly similar to CGHU7L collagen	hi-lo-hi
80	104978	AI199268	Hs.111334	ESTs, Weakly similar to CGHU7L collagen	hi-lo-hi
	129626	F13272	Hs.31097	ferritin, light polypeptide	hi-lo-hi
	118895	BE304917	Hs.27769	hypothetical protein FLJ21478	hi-lo-hi
	332577	AI826268	Hs.165909	ESTs, Weakly similar to MCAT_HUMAN MITOC	hi-lo-hi
	116732	AW152225	Hs.14587	ESTs	hi-lo-hi
	106774	AI216748	Hs.303116	ESTs, Weakly similar to AF151859 1 CGI-1	hi-lo-hi
	108818	BE612676		stromal cell-derived factor 2-like 1	hi-lo-hi

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5	315618	AI287341	"Hs.154029	bHLH factor Hes4	hi-lo-hi
	110561	AA379597	Hs.5199	HSPC150 protein similar to ubiquitin-con	hi-lo-hi
	132959	AW014195	Hs.61472	ESTs, Weakly similar to unknown [S.cerev	hi-lo-hi
	103195	AA351547	Hs.2642	eukaryotic translation elongation factor	hi-lo-hi
	100368	D79987	Hs.153479	extra spindle poles, S. cerevisiae, homo	hi-lo-hi
10	103177	BE244377	"Hs.48876	farnesyl-diphosphate farnesyltransferase	hi-lo-hi
	109141	AF174600	Hs.193360	F-box protein Fbx20	hi-lo-hi
	100676	X02761	"Hs.287820	fibronectin 1	hi-lo-hi
	100254	AA452181	Hs.77643	FK506-binding protein 1B (12.6 kD)	hi-lo-hi
	133688	U71321	Hs.7557	FK506-binding protein 5	hi-lo-hi
15	107129	AC004770	"Hs.4756	flap structure-specific endonuclease 1	hi-lo-hi
	102696	BE540274	Hs.239	forkhead box M1	hi-lo-hi
	101753	L11144	Hs.1907	galanin	hi-lo-hi
	101597	AA317089	"Hs.597	glutamic-oxaloacetic transaminase 1, sol	hi-lo-hi
	133512	L18861		gb:Human Goli-mbp gene, exon 1.	hi-lo-hi
20	130080	X14850	Hs.147057	H2A histone family, member X	hi-lo-hi
	101600	BE561617	"Hs.119192	H2A histone family, member Z	hi-lo-hi
	101332	J04088	"Hs.156346	topoisomerase (DNA) II alpha (170kD)	hi-lo-hi
	132957	AA316181	Hs.61635	six transmembrane epithelial antigen of	hi-lo-hi
	129726	H15474	Hs.132898	fatty acid desaturase 1	hi-lo-hi
25	106925	AK002011	Hs.37558	hypothetical protein FLJ11149	hi-lo-hi
	105643	BE621719	Hs.173802	KIAA0603 gene product	hi-lo-hi
	116028	H59799	Hs.42644	thioredoxin-like	hi-lo-hi
	105437	AF151076	Hs.25199	hypothetical protein	hi-lo-hi
	122512	AF053305	Hs.98658	budding uninhibited by benzimidazoles 1	hi-lo-hi
30	131991	AF053306	Hs.36708	budding uninhibited by benzimidazoles 1	hi-lo-hi
	135015	AW361638	Hs.278336	LGN protein	hi-lo-hi
	102208	U22961		gb:Human mRNA clone with similarity to L	hi-lo-hi
	100144	AL119964	Hs.75616	seladin-1	hi-lo-hi
	100447	NM_014767	Hs.74583	KIAA0275 gene product	hi-lo-hi
35	116578	D21262	Hs.75337	nucleolar phosphoprotein p130	hi-lo-hi
	130350	AA369601	Hs.239138	pre-B-cell colony-enhancing factor	hi-lo-hi
	101045	J05614		gb:Human proliferating cell nuclear anti	hi-lo-hi
	101544	M31169		gb:Human propionyl-CoA carboxylase beta-	hi-lo-hi
	113674	NM_014214	Hs.5753	inositol(myo)-1(or 4)-monophosphatase 2	hi-lo-hi
40	102260	AL039104	Hs.159557	karyopherin alpha 2 (RAG cohort 1, impor	hi-lo-hi
	100154	H60720	Hs.81892	KIAA0101 gene product	hi-lo-hi
	100199	BE562298	Hs.71827	KIAA0112 protein; homolog of yeast ribos	hi-lo-hi
	100372	NM_014791	Hs.184339	KIAA0175 gene product	hi-lo-hi
	100387	D83777	"Hs.75137	KIAA0193 gene product	hi-lo-hi
45	131514	BE270734	"Hs.2795	lactate dehydrogenase A	hi-lo-hi
	102938	W27518	Hs.234489	lactate dehydrogenase B	hi-lo-hi
	105811	BE617695	Hs.285192	protein phosphatase 1, regulatory (inhib	hi-lo-hi
	101013	BE300094	"Hs.227751	lectin, galactoside-binding, soluble, 1	hi-lo-hi
	124148	BE300094	"Hs.227751	lectin, galactoside-binding, soluble, 1	hi-lo-hi
50	102968	AU075611	Hs.154672	methylene tetrahydrofolate dehydrogenase	hi-lo-hi
	130149	AW067805	Hs.172665	methylene tetrahydrofolate dehydrogenase	hi-lo-hi
	114767	AI859865	Hs.154443	minichromosome maintenance deficient (S.	hi-lo-hi
	129168	AI132988	Hs.109052	chromosome 14 open reading frame 2	hi-lo-hi
	105011	BE091926	Hs.16244	mitotic spindle coiled-coil related prot	hi-lo-hi
55	103023	AW500470	Hs.117950	multifunctional polypeptide similar to S	hi-lo-hi
	102808	BE242818	"Hs.179606	nuclear RNA helicase, DECD variant of DE	hi-lo-hi
	318617	AW247252	Hs.75514	nucleoside phosphorylase	hi-lo-hi
	101568	M81740	Hs.75212	ornithine decarboxylase 1	hi-lo-hi
	102076	BE299197	Hs.179665	cyclin-dependent kinase inhibitor 1A (p2	hi-lo-hi
60	100202	BE294407	"Hs.99910	phosphofructokinase, platelet	hi-lo-hi
	101032	BE208854	Hs.46039	phosphoglycerate mutase 2 (muscle)	hi-lo-hi
	130553	AF062649	"Hs.252587	pituitary tumor-transforming 1	hi-lo-hi
	101626	M57399	Hs.44	pleiotrophin (heparin binding growth fac	hi-lo-hi
	101992	X90725	Hs.77597	polo (Drosophila)-like kinase	hi-lo-hi
65	132164	AI752235	Hs.41270	procollagen-lysine, 2-oxoglutarate 5-dio	hi-lo-hi
	101396	BE267931	"Hs.78996	proliferating cell nuclear antigen	hi-lo-hi
	119018	AA631143	Hs.179809	ESTs	hi-lo-hi
	101840	AA236291	Hs.183583	serine (or cysteine) proteinase inhibito	hi-lo-hi
	332640	BE568452	Hs.5101	protein regulator of cytokinesis 1	hi-lo-hi
70	132543	BE568452	Hs.5101	protein regulator of cytokinesis 1	hi-lo-hi
	101118	AA371931	"Hs.77422	proteolipid protein 2 (colonic epitheliu	hi-lo-hi
	109166	AA219691	Hs.73625	RAB6 interacting, kinesin-like (rabkines	hi-lo-hi
	100830	AC004770	"Hs.4756	flap structure-specific endonuclease 1	hi-lo-hi
	107059	BE614410	Hs.23044	RAD51 (S. cerevisiae) homolog (E coli Re	hi-lo-hi
75	321693	AA227069	Hs.173737	ras-related C3 botulinum toxin substrate	hi-lo-hi
	101148	NM_002923	Hs.78944	regulator of G-protein signalling 2, 24k	hi-lo-hi
	130567	AA383092	Hs.1608	replication protein A3 (14kD)	hi-lo-hi
	103076	NM_001034	Hs.75319	ribonucleotide reductase M2 polypeptide	hi-lo-hi
	103131	BE536069	Hs.2962	S100 calcium-binding protein P	hi-lo-hi
80	102212	AW411491	Hs.75069	serine hydroxymethyltransferase 2 (mitoc	hi-lo-hi
	104254	AW411425	Hs.180655	serine/threonine kinase 12	hi-lo-hi
	102748	BE018138	Hs.24447	sigma receptor (SR31747 binding protein	hi-lo-hi
	102012	BE259035	Hs.118400	singed (Drosophila)-like (sea urchin fas	hi-lo-hi
	102522	BE250944	Hs.183556	solute carrier family 1 (neutral amino a	hi-lo-hi
	132994	AA112748	Hs.279905	clone HQ0310 PRO0310p1	hi-lo-hi
	101971	Z49105	"Hs.289105	synovial sarcoma, X breakpoint 2	hi-lo-hi

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5	126645	AA316181	Hs.61635	six transmembrane epithelial antigen of	hi-lo-hi
	103058	X57348	Hs.184510	stratlin	hi-lo-hi
	102632	U66618	Hs.250581	SWI/SNF related, matrix associated, acti	hi-lo-hi
	103269	AF230662	"Hs.289105	synovial sarcoma, X breakpoint 2	hi-lo-hi
	128920	AA622037	Hs.166468	programmed cell death 5	hi-lo-hi
10	100114	X02308	Hs.82962	thymidylate synthetase	hi-lo-hi
	102846	BE264974	Hs.6566	thyroid hormone receptor interactor 13	hi-lo-hi
	131877	J04088	"Hs.156346	topoisomerase (DNA) II alpha (170kD)	hi-lo-hi
	100866	U14134	Hs.75113	general transcription factor IIIA	hi-lo-hi
	133893	AI434699	Hs.77356	transferrin receptor (p90, CD71)	hi-lo-hi
15	130135	AA311426	"Hs.21635	tubulin, gamma 1	hi-lo-hi
	130287	AA479005	Hs.154036	tumor suppressing subtransferable candid	hi-lo-hi
	126180	L32977	Hs.3712	ubiquinol-cytochrome c reductase, Rieske	hi-lo-hi
	101536	NM_006002	Hs.77917	ubiquitin carboxyl-terminal esterase L3	hi-lo-hi
	102687	NM_007019	"Hs.93002	ubiquitin carrier protein E2-C	hi-lo-hi
20	103556	Z19002	Hs.37096	zinc finger protein 145 (Kruppel-like, e	hi-lo-hi
	300022				hi-lo-hi-lo
	133015	AJ002744	Hs.246315	UDP-N-acetyl-alpha-D-galactosamine:polyp	hi-lo-hi-lo
	129642	NM_001360	Hs.11806	7-dehydrocholesterol reductase	hi-lo-lo
	134369	AF207664	Hs.8230	a disintegrin-like and metalloprotease (hi-lo-lo
25	300023				hi-lo-lo
	125183	AV660804	Hs.301417	AHNAK nucleoprotein (desmoyokin)	hi-lo-lo
	101766	M60899	"Hs.301417	AHNAK nucleoprotein (desmoyokin)	hi-lo-lo
	133616	BE265133	"Hs.217493	annexin A2	hi-lo-lo
	102146	AW162057	Hs.78629	ATPase, Na+/K+ transporting, beta 1 poly	hi-lo-lo
30	318538	AI750979	Hs.74034	Homo sapiens clone 24651 mRNA sequence	hi-lo-lo
	103554	AI878826	Hs.323469	caveolin 1, caveolae protein, 22kD	hi-lo-lo
	329365			CHX_hs gj15868838	hi-lo-lo
	334282			CH22_FGENES.369_12	hi-lo-lo
	334891			CH22_FGENES.452_5	hi-lo-lo
35	335149			CH22_FGENES.499_5	hi-lo-lo
	335682			CH22_FGENES.595_2	hi-lo-lo
	335756			CH22_FGENES.604_5	hi-lo-lo
	303951	AW475081	Hs.172928	collagen, type I, alpha 1	hi-lo-lo
	134421	AU077196	Hs.82985	collagen, type V, alpha 2	hi-lo-lo
40	131101	BE387561	Hs.22981	DKFZP586M1523 protein	hi-lo-lo
	124153	AU077333	"Hs.160483	erythrocyte membrane protein band 7.2 (s	hi-lo-lo
	103328	AU077333	"Hs.160483	erythrocyte membrane protein band 7.2 (s	hi-lo-lo
	322035	AL137517	"Hs.306201	hypothetical protein DKFZp564O1278	hi-lo-lo
	301872	H84730	Hs.326391	ESTs, Highly similar to KIAA1437 protein	hi-lo-lo
45	303820	AB037858	Hs.173484	hypothetical protein FLJ10337	hi-lo-lo
	304049	T58155		gb:yb98h03.s1 Stratagene lung (937210) H	hi-lo-lo
	304735	AA576453		gb:nm75h11.s1 NCLCGAP_Co9 Homo sapiens	hi-lo-lo
	306999	AI138628	Hs.308058	EST, Weakly similar to zinc finger prot	hi-lo-lo
	128789	AW368576	Hs.139851	caveolin 2	hi-lo-lo
50	132057	AB037858	Hs.173484	hypothetical protein FLJ10337	hi-lo-lo
	114795	AB037858	Hs.173484	hypothetical protein FLJ10337	hi-lo-lo
	104204	AK001691	Hs.57655	hypothetical protein FLJ10829	hi-lo-lo
	105200	AA328102	Hs.24641	cytoskeleton associated protein 2	hi-lo-lo
	105493	AL047586	Hs.10283	RNA binding motif protein 8B	hi-lo-lo
55	107977	AI188161	Hs.144627	ESTs	hi-lo-lo
	108880	AA766605	"Hs.47099	hypothetical protein FLJ21212	hi-lo-lo
	111157	AL109729	Hs.18948	ESTs, Highly similar to A31026 probable	hi-lo-lo
	116202	BE159395	Hs.87089	ESTs	hi-lo-lo
	120689	AW134519	Hs.96125	ESTs	hi-lo-lo
60	121847	AA446628	Hs.2799	cartilage linking protein 1	hi-lo-lo
	124182	AI637471	Hs.107801	ESTs	hi-lo-lo
	126515	BE395085	Hs.10086	type I transmembrane protein Fm14	hi-lo-lo
	130466	W19744	Hs.180059	Homo sapiens cDNA FLJ20653 fis, clone KA	hi-lo-lo
	131076	AA749230	Hs.22666	ESTs	hi-lo-lo
65	131084	NM_017413	Hs.303084	apelin; peptide ligand for APJ receptor	hi-lo-lo
	134109	AA348031	Hs.7913	ESTs	hi-lo-lo
	300258	AI478933	Hs.188260	ESTs	hi-lo-lo
	302767	H84900	Hs.17882	ESTs	hi-lo-lo
	312391	R43707	Hs.133159	ESTs, Weakly similar to PIHUSD salivary	hi-lo-lo
70	312689	AW450461	Hs.203985	ESTs	hi-lo-lo
	315715	AI284219	Hs.130749	ESTs	hi-lo-lo
	315843	AA679430	Hs.191897	ESTs	hi-lo-lo
	322447	AI735759	Hs.52620	integrin, beta 8	hi-lo-lo
	322826	AI807893	Hs.201771	ESTs	hi-lo-lo
75	324867	AI624707	"Hs.5921	Homo sapiens cDNA: FLJ21582 fis, clone C	hi-lo-lo
	331336	AA287450	Hs.93842	Homo sapiens cDNA: FLJ22554 fis, clone	hi-lo-lo
	331353	AA953006	Hs.88143	ESTs	hi-lo-lo
	133063	AI654133	Hs.30212	thyroid receptor interacting protein 15	hi-lo-lo
	311034	BE567130	Hs.311389	ESTs, Moderately similar to PT0375 natur	hi-lo-lo
80	108647	BE546947	Hs.44276	homeo box C10	hi-lo-lo
	124955	AA376768	"Hs.324841	hypothetical protein FLJ22622	hi-lo-lo
	113923	AW953484	Hs.3849	hypothetical protein FLJ22041 similar to	hi-lo-lo
	310657	AI431798	Hs.164192	ESTs, Weakly similar to Y161_HUMAN HYPOT	hi-lo-lo
	302943	AI581344	Hs.127812	ESTs, Weakly similar to T17330 hypotheti	hi-lo-lo
	128453	X02761	"Hs.287820	fibronectin 1	hi-lo-lo
	305232	AA670052	Hs.169476	glyceraldehyde-3-phosphate dehydrogenase	hi-lo-lo

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5	117642	U55184	"Hs.154145	hypothetical protein FLJ11585	hi-lo-lo
	115881	NM_005756	Hs.184942	G protein-coupled receptor 64	hi-lo-lo
	133666	U56725	Hs.75452	heat shock 70kD protein 2	hi-lo-lo
	103262	X78565	Hs.289114	hexabrachion (tenascin C, cyclotactin)	hi-lo-lo
	100793	S69027		gb:HCX C6=class I homeodomain {fragment	hi-lo-lo
10	102289	U32114			hi-lo-lo
	319109	Z45662	Hs.90797	Homo sapiens clone 23620 mRNA sequence	hi-lo-lo
	116357	AF052107	Hs.90797	Homo sapiens clone 23620 mRNA sequence	hi-lo-lo
	101497	W05150	"Hs.37034	homeo box A5	hi-lo-lo
	105508	AA173942	Hs.326416	Homo sapiens mRNA; cDNA DKFZp564H1916 (f	hi-lo-lo
15	302290	AA179949	Hs.175563	Homo sapiens mRNA; cDNA DKFZp564N0763 (f	hi-lo-lo
	102838	R34657	Hs.80658	uncoupling protein 2 (mitochondrial, pro	hi-lo-lo
	100235	D29954	Hs.13421	KIAA0056 protein	hi-lo-lo
	133507	NM_002206	Hs.74369	integrin, alpha 7	hi-lo-lo
	125573	AI351642	Hs.182241	interferon induced transmembrane protein	hi-lo-lo
20	103059	X57351	Hs.174195	interferon induced transmembrane protein	hi-lo-lo
	330415	D83777	"Hs.75137	KIAA0193 gene product	hi-lo-lo
	303054	BE265848	Hs.289090	colon cancer-associated protein Mic1	hi-lo-lo
	133579	X75346	Hs.75074	mitogen-activated protein kinase-activat	hi-lo-lo
	100528	BE386801	Hs.21858	trinucleotide repeat containing 3	hi-lo-lo
25	107480	AF001691	Hs.74304	periplakin	hi-lo-lo
	133050	X73424	Hs.63788	propionyl Coenzyme A carboxylase, beta p	hi-lo-lo
	133061	AI186431	Hs.296638	prostate differentiation factor	hi-lo-lo
	106390	AJ297436	Hs.20166	prostate stem cell antigen	hi-lo-lo
	302124	AA676403	Hs.145078	regulator of differentiation (in S. pom	hi-lo-lo
30	129823	X00949	"Hs.105314	relaxin 1 (H1)	hi-lo-lo
	134444	BE184455	"Hs.251754	secretory leukocyte protease inhibitor (hi-lo-lo
	103240	U81961	Hs.2794	sodium channel, nonvoltage-gated 1 alpha	hi-lo-lo
	115761	AA366037	Hs.90911	solute carrier family 16 (monocarboxylic	hi-lo-lo
	321412	AI674383	Hs.22891	solute carrier family 7 (cationic amino	hi-lo-lo
35	126487	AA283309	Hs.184601	solute carrier family 7 (cationic amino	hi-lo-lo
	101759	M80244	Hs.184601	solute carrier family 7 (cationic amino	hi-lo-lo
	112941	AW163034	Hs.6467	synaptogyrin 3	hi-lo-lo
	134351	BE272506	"Hs.82109	syndecan 1	hi-lo-lo
	125924	BE272506	"Hs.82109	syndecan 1	hi-lo-lo
40	130982	AA033627	Hs.21858	trinucleotide repeat containing 3	hi-lo-lo
	133473	AW301993	Hs.73980	troponin T1, skeletal, slow	hi-lo-lo
	101042	T46839	"Hs.10319	UDP glycosyltransferase 2 family, polype	hi-lo-lo
	129565	X77777	Hs.198726	vasoactive intestinal peptide receptor 1	hi-lo-lo
	102992	M85430	"Hs.155191	villin 2 (ezrin)	hi-lo-lo
45	106868	BE185536	Hs.300816	Homo sapiens mRNA; cDNA DKFZp564I172 (fr	lo-hi-lo
	132618	AL050025	"Hs.279916	hypothetical protein FLJ20151	lo-hi-hi
	100187	D17793	"Hs.78183	aldo-keto reductase family 1, member C3	lo-hi-hi
	116334	AL038450	Hs.48948	ATP2C1 calcium transport ATPase, same as	lo-hi-hi
	134454	NM_013230	Hs.286124	CD24 antigen (small cell lung carcinoma	lo-hi-hi
50	302067	BE542706	Hs.222399	CEGP1 protein	lo-hi-hi
	105500	AW602166	Hs.222399	CEGP1 protein	lo-hi-hi
	100732	AA557680	"Hs.76152	decorin	lo-hi-hi
	129265	AA530892	Hs.171695	dual specificity phosphatase 1	lo-hi-hi
	117789	N48294	Hs.46850	EST	lo-hi-hi
55	330786	BE379594	"Hs.49136	ESTs, Moderately similar to ALU7_HUMAN A	lo-hi-hi
	319808	T58960	Hs.17283	hypothetical protein FLJ10890	lo-hi-hi
	303502	BE174240		gb:QV1-HT0573-290200-092-f06 HT0573 Homo	lo-hi-hi
	116780	H22566	"Hs.30098	ESTs	lo-hi-hi
	104189	AB040927	Hs.301804	KIAA1494 protein	lo-hi-hi
60	105588	L43821	Hs.80261	enhancer of filamentation 1 (cas-like do	lo-hi-hi
	105731	AA834684	Hs.29131	nuclear receptor coactivator 2	lo-hi-hi
	105772	H57111	Hs.221132	ESTs	lo-hi-hi
	105794	H24530	Hs.273294	hypothetical protein FLJ20069	lo-hi-hi
	113098	N77737	Hs.8349	ApoBec-1 complementation factor; APOBEC-	lo-hi-hi
65	113803	AW880709	"Hs.283683	chromosome 8 open reading frame 4	lo-hi-hi
	114530	AA601038	Hs.191797	ESTs	lo-hi-hi
	116188	AA468183	Hs.184598	Homo sapiens cDNA: FLJ23241 fis, clone C	lo-hi-hi
	117330	AI904095	Hs.43423	ESTs	lo-hi-hi
	117701	BE063921	Hs.295971	ESTs	lo-hi-hi
70	120911	AI189754	Hs.144330	ESTs	lo-hi-hi
	124083	AW195237	Hs.7734	hypothetical protein FLJ22174	lo-hi-hi
	124690	AW883529	Hs.173830	ESTs	lo-hi-hi
	130796	AA088309	Hs.19525	hypothetical protein FLJ22794	lo-hi-hi
	131524	AB040927	Hs.301804	KIAA1494 protein	lo-hi-hi
75	132116	AW960474	Hs.40289	ESTs	lo-hi-hi
	132442	AW970859	Hs.313503	ESTs	lo-hi-hi
	310219	AI221087	Hs.147761	ESTs	lo-hi-hi
	310598	AI439136	Hs.140546	ESTs	lo-hi-hi
	310884	AW014684	Hs.232189	ESTs	lo-hi-hi
80	311587	AI828254	Hs.271019	ESTs, Weakly similar to SMN1_HUMAN SURV	lo-hi-hi
	312240	R36475	Hs.24321	Homo sapiens cDNA FLJ12028 fis, clone HE	lo-hi-hi
	312803	AA677934	Hs.117864	ESTs	lo-hi-hi
	314219	AA262331	Hs.48376	Homo sapiens clone HB-2 mRNA sequence	lo-hi-hi
	315052	AA876910	Hs.134427	ESTs	lo-hi-hi
	331919	AA446889	Hs.119316	ESTs	lo-hi-hi
	133240	AK001489	Hs.242894	ADP-ribosylation factor-like 1	lo-hi-hi

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5	134006	Z45957	Hs.7837	G-protein-coupled receptor induced prote	lo-hi-hi
	124847	W07701	"Hs.304177	Homo sapiens clone FLB8503 PRO2286 mRNA,	lo-hi-hi
	129087	AI348027	Hs.108557	Homo sapiens clone PP1057 unknown mRNA	lo-hi-hi
	131762	AA744902	"Hs.107767	hypothetical protein PRO1489	lo-hi-hi
	129000	AA744902	"Hs.107767	hypothetical protein PRO1489	lo-hi-hi
10	105713	AI122843	"Hs.184319	ESTs, Weakly similar to KIAA1006 protein	lo-hi-hi
	118475	N66845		gb:za46c11.s1 Soares fetal liver spleen	lo-hi-hi
	118381	N64513	Hs.48994	ESTs, Weakly similar to AF151800 1 CGI-4	lo-hi-hi
	105057	AA134233		gb:zo20f10.s1 Stratagene colon (937204)	lo-hi-hi
	131507	AI826268	Hs.27769	ESTs, Weakly similar to MCAT_HUMAN MITOC	lo-hi-hi
15	124970	BE272662	Hs.106534	hypothetical protein FLJ22625	lo-hi-hi
	130094	NM_001471	"Hs.167017	gamma-aminobutyric acid (GABA) B recepto	lo-hi-hi
	302357	X03178	Hs.198246	group-specific component (vitamin D bind	lo-hi-hi
	113231	AA278583	Hs.180737	Homo sapiens clone 23664 and 23905 mRNA	lo-hi-hi
	111923	BE363234	Hs.25925	Homo sapiens clone 23880 mRNA sequence	lo-hi-hi
20	128530	AI932995	Hs.183475	Homo sapiens clone 25061 mRNA sequence	lo-hi-hi
	128987	AI339046	Hs.107637	hypothetical protein FLJ12806	lo-hi-hi
	315368	AB037745	Hs.104696	KIAA1324 protein	lo-hi-hi
	133944	AW068579	Hs.7780	Homo sapiens mRNA; cDNA DKFZp564A072 (fr	lo-hi-hi
	115084	BE383668	"Hs.42484	hypothetical protein FLJ10618	lo-hi-hi
25	132883	AA373314	Hs.5897	Homo sapiens mRNA; cDNA DKFZp586P1822 (f	lo-hi-hi
	109623	AW207385	Hs.295901	KIAA0493 protein	lo-hi-hi
	130577	M69241	"Hs.162	insulin-like growth factor binding prote	lo-hi-hi
	101899	AF188747	"Hs.181350	kalikrein 2, prostatic	lo-hi-hi
	130336	AA535210	"Hs.171995	kalikrein 3, (prostate specific antigen	lo-hi-hi
30	128180	AW949068	Hs.171995	kalikrein 3, (prostate specific antigen	lo-hi-hi
	134921	AL137491	Hs.125511	Homo sapiens mRNA; cDNA DKFZp434P1530 (f	lo-hi-hi
	302385	AJ224172	Hs.204066	lipophilin B (uteroglobin family member)	lo-hi-hi
	117921	AA021459	Hs.306480	Homo sapiens mRNA; cDNA DKFZp761E2112 (f	lo-hi-hi
	101701	NM_002436	Hs.1861	membrane protein, palmitoylated 1 (55kD)	lo-hi-hi
35	130356	AF127577	Hs.155017	nuclear receptor interacting protein 1	lo-hi-hi
	101763	AB001914	Hs.170414	paired basic amino acid cleaving system	lo-hi-hi
	130342	U81802	Hs.154846	phosphatidylinositol 4-kinase, catalytic	lo-hi-hi
	130760	AW379130	Hs.18953	phosphodiesterase 9A	lo-hi-hi
	101461	N98569	Hs.76422	phospholipase A2, group IIA (platelets,	lo-hi-hi
40	134032	NM_005025	Hs.78589	serine (or cysteine) proteinase inhibito	lo-hi-hi
	303762	AF034799	Hs.30981	protein tyrosine phosphatase, receptor t	lo-hi-hi
	110932	AA021459	Hs.306480	Homo sapiens mRNA; cDNA DKFZp761E2112 (f	lo-hi-hi
	135192	U83993	Hs.321709	purinergic receptor P2X, ligand-gated io	lo-hi-hi
	133886	U97276	Hs.77266	quiescin Q6	lo-hi-hi
45	134142	BE244053	Hs.79362	retinoblastoma-like 2 (p130)	lo-hi-hi
	100877	X80821	Hs.302177	H.sapiens mRNA for ribosomal protein L18	lo-hi-hi
	133534	AU077115	Hs.201675	RNA binding motif protein 5	lo-hi-hi
	133011	NM_006379	Hs.171921	sema domain, immunoglobulin domain (lg),	lo-hi-hi
	132150	W26406	Hs.295923	seven in absentia (Drosophila) homolog 1	lo-hi-hi
50	103110	X62822	Hs.2554	sialyltransferase 1 (beta-galactoside al	lo-hi-hi
	130173	U38847	Hs.151518	TAR (HIV) RNA-binding protein 1	lo-hi-hi
	127435	X69086	"Hs.286161	Homo sapiens cDNA FLJ13613 fis, clone PL	lo-hi-hi
	110520	N54069	Hs.4082	lectin, galactoside-binding, soluble, 8	lo-hi-hi
	114660	AA071383		gb:zm61c05.r1 Stratagene fibroblast (937	lo-hi-hi
55	330541	NM_002038	Hs.285827	interferon, alpha-inducible protein (clo	lo-hi-hi
	101486	AA506324	Hs.1852	acid phosphatase, prostate	lo-hi-hi
	332396	NM_000481	Hs.102	aminomethyltransferase (glycine cleavage	lo-hi-hi
	100559	AA535210	"Hs.171995	kalikrein 3, (prostate specific antigen	lo-hi-hi
	134738	AU076801	Hs.89436	cadherin 17, LI cadherin (liver-intestin	lo-hi-hi
60	103119	X63629	Hs.2877	cadherin 3, type 1, P-cadherin (placenta	lo-hi-hi
	302892	AW176909	Hs.42346	calcineurin-binding protein calsarcin-1	lo-hi-hi
	105402	AB014680	Hs.3796	carbohydrate (chondroitin 6/keratan) sul	lo-hi-hi
	102976	AU077174	"Hs.288181	cathepsin H	lo-hi-hi
	101793	W01076	"Hs.119663	CD59 antigen p18-20 (antigen identified	lo-hi-hi
65	129890	AI868872	"Hs.282804	Homo sapiens cDNA: FLJ22704 fis, clone H	lo-hi-hi
	328164			CH.06_hs_gli588068	lo-hi-hi
	328648			CH.07_hs_gli6004473	lo-hi-hi
	330032			CH.16_p2_gli6682596	lo-hi-hi
	330033			CH.16_p2_gli6682596	lo-hi-hi
70	326816			CH.20_hs_gli6552458	lo-hi-hi
	337603			CH22_C20H12.GENSCAN.16-2	lo-hi-hi
	338561			CH22_EM:AC005500.GENSCAN.421-5	lo-hi-hi
	338562			CH22_EM:AC005500.GENSCAN.421-6	lo-hi-hi
	333743			CH22_FGENES.264_1	lo-hi-hi
75	333845			CH22_FGENES.290_3	lo-hi-hi
	333849			CH22_FGENES.290_8	lo-hi-hi
	334221			CH22_FGENES.360_1	lo-hi-hi
	334222			CH22_FGENES.360_3	lo-hi-hi
	334578			CH22_FGENES.406_1	lo-hi-hi
80	336662			CH22_FGENES.41-1	lo-hi-hi
	336684			CH22_FGENES.46-1	lo-hi-hi
	335289			CH22_FGENES.527_2	lo-hi-hi
	335290			CH22_FGENES.527_3	lo-hi-hi
	335293			CH22_FGENES.527_6	lo-hi-hi
	337182			CH22_FGENES.570-2	lo-hi-hi
	335809			CH22_FGENES.617_6 (same as BFH4)	lo-hi-hi

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	335810		CH22_FGENES.617_7	lo-hi-lo
	335824		CH22_FGENES.619_11 (same as BFH5)	lo-hi-lo
	336054		CH22_FGENES.683_3	lo-hi-lo
	333124		CH22_FGENES.81_8	lo-hi-lo
5	332340	AP000692	Hs.129781	chromosome 21 open reading frame 5
	130380	AI949359	Hs.143600	type II Golgi membrane protein
	102962	R50032	Hs.159263	collagen, type VI, alpha 2
	331306	AF102546	Hs.63931	dachshund (Drosophila) homolog
10	319408	AA448090	Hs.87359	ESTs, Highly similar to RB18 MOUSE RAS-R
	312197	T96203		gb:ye48b07.r1 Soares fetal liver spleen
	312405	AI523875		gb:tg97d04.x1 NCI_CGAP_CLL1 Homo sapiens
	312939	AA495830	Hs.24444	Homo sapiens cDNA: FLJ22165 fis, clone H
	313475	AA010200	Hs.175561	ESTs
15	313624	AA525775	Hs.292523	ESTs
	316897	AA838114	Hs.221612	ESTs
	317850	AI681545	Hs.152982	hypothetical protein FLJ13117
	318541	T30290	Hs.107515	ESTs
	321325	AB033100	Hs.300646	KIAA protein (similar to mouse paladin)
20	321696	AA628791	Hs.76228	amplified in osteosarcoma
	322189	H65014		gb:yu68f10.r1 Weizmann Olfactory Epithel
	322463	AI242754	Hs.137306	ESTs
	322540	R76593		gb:yi60c11.r1 Soares placenta Nb2HP Homo
	323131	AK002088	Hs.270124	Homo sapiens cDNA FLJ11226 fis, clone PL
	323243	W47525	Hs.110771	Homo sapiens cDNA: FLJ21904 fis, clone H
25	323591	AA301270		gb:EST14192 Testis tumor Homo sapiens cD
	323753	AK002161	Hs.70266	yeast Sec31p homolog
	323835	AL042005	Hs.11117	tripeptidyl peptidase II
	323926	AA354572		gb:EST62857 Jurkat T-cells V Homo sapien
	324047	AI433357	*Hs.271340	ESTs
30	324330	AA884766		gb:am20a10.s1 Soares_NFL_T_GBC_S1 Homo s
	324753	AA612626	Hs.144871	Homo sapiens cDNA FLJ13752 fis, clone PL
	300702	AA075481	Hs.111334	ferritin, light polypeptide
	301712	BE083080	Hs.274323	Homo sapiens, Similar to sialyltransfera
35	302380	AA325533	Hs.136102	KIAA0853 protein
	302970	W05608	Hs.312679	EST
	303187	AA115962	Hs.323423	ESTs, Moderately similar to B Chain B,
	303194	AA082000		gb:zn26f07.r1 Stratagene neuroepithelium
	305612	AA782347	Hs.272572	hemoglobin, alpha 2
40	304263	AA062837		gb:zm05b11.s1 Stratagene corneal stroma
	304275	AA070605		gb:zm53h09.s1 Stratagene fibroblast (937
	304309	AA112147		gb:zm64c06.s1 Stratagene fibroblast (937
	305503	AA759177	Hs.298148	ESTs, Weakly similar to KIAA0565 protei
	306615	AK000142	Hs.101774	hypothetical protein FLJ23045
45	309390	AW080585		gb:xc33f09.x1 NCI_CGAP_Co18 Homo sapiens
	104667	AI239923	Hs.30098	ESTs
	310014	D60745	Hs.25925	Homo sapiens clone 23860 mRNA sequence
	318814	W07361	Hs.22545	Homo sapiens cDNA FLJ12935 fis, clone NT
	321896	C04863	Hs.47191	ESTs
50	331661	W52448	Hs.56147	ESTs
	332120	AA609684	Hs.112748	Homo sapiens cDNA: FLJ21543 fis, clone C
	332256	AW975028	Hs.102754	ESTs
	107252	D60745	Hs.25925	Homo sapiens clone 23860 mRNA sequence
	112068	AI264847	Hs.22545	Homo sapiens cDNA FLJ12935 fis, clone NT
55	117929	N51075	Hs.47191	ESTs
	119637	W52448	Hs.56147	ESTs
	123712	AA609684	Hs.112748	Homo sapiens cDNA: FLJ21543 fis, clone C
	124560	AW975028	Hs.102754	ESTs
	105039	AA907305	Hs.36475	ESTs
60	105271	AA807881	Hs.25329	ESTs
	106689	AW296584	Hs.293782	ESTs
	106849	AL137281	Hs.17110	Homo sapiens mRNA; cDNA DKFZp434C2016 (f
	107071	AW385224	Hs.35198	ectonucleotide pyrophosphatase/phosphodi
	108218	W57550	Hs.301526	hypothetical protein FLJ13181
65	110930	BE242691	Hs.14947	ESTs, Weakly similar to ALU1_HUMAN ALU S
	112098	R44714	Hs.106795	Homo sapiens cDNA FLJ13136 fis, clone NT
	112170	BE246743	Hs.288529	hypothetical protein FLJ22635
	112902	AL035633	*Hs.129190	Human DNA sequence from clone RP5-1046G1
	114877	AW024162	Hs.205125	ESTs
70	116312	BE379794	Hs.65403	hypothetical protein
	116739	H01463	Hs.93534	ESTs
	119267	AA064970	Hs.118145	ESTs
	120570	AA280679	Hs.271445	ESTs, Weakly similar to ALU1_HUMAN ALU
	121176	AL121523	Hs.97774	ESTs
75	123360	AA532718	Hs.178604	ESTs
	123974	NM_015678	Hs.3821	neurobeachin
	124777	R41933		gb:yg04f09.s1 Soares Infant brain 1N1B H
	128046	AA873285		gb:oh68h05.s1 NCI_CGAP_Kid5 Homo sapiens
80	128666	AA808466	Hs.103395	hypothetical protein FLJ14146
	130639	AI557212	*Hs.17132	ESTs
	130693	R68537	Hs.17962	ESTs
	131756	AA443966	Hs.31595	ESTs
	131985	AA503020	Hs.36563	hypothetical protein FLJ22418

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5	132932	AW118826	Hs.6093	Homo sapiens cDNA: FLJ22763 fis, clone K	lo-hi-lo
	134696	BE326276	"Hs.8861	ESTs	lo-hi-lo
	300967	AA565209	Hs.269439	ESTs	lo-hi-lo
	301182	AW291411	Hs.192531	ESTs, Weakly similar to S00754 zinc fing	lo-hi-lo
	302595	AI699372	Hs.193247	Homo sapiens mRNA; cDNA DKFZp434A171 (fr	lo-hi-lo
10	303132	AI929819	Hs.4055	chromosome 21 open reading frame 50	lo-hi-lo
	303506	AA340606	Hs.105387	ESTs, Weakly similar to Homolog of rat Z	lo-hi-lo
	303654	BE246743	Hs.288529	hypothetical protein FLJ22635	lo-hi-lo
	310026	AA278233	Hs.100891	ESTs	lo-hi-lo
	310056	AI253072	Hs.145383	ESTs	lo-hi-lo
15	310353	AI261700	Hs.145544	ESTs	lo-hi-lo
	310371	AI262584	Hs.145575	ESTs	lo-hi-lo
	310430	AI670843	Hs.200257	ESTs	lo-hi-lo
	310438	AW022192	Hs.200197	ESTs	lo-hi-lo
	310455	AI277603	Hs.145990	ESTs	lo-hi-lo
20	310787	AW262580	Hs.147674	KIAA1621 protein	lo-hi-lo
	311067	AI587332	Hs.209115	ESTs	lo-hi-lo
	311422	F00677	Hs.101316	ESTs	lo-hi-lo
	311465	AI758660	Hs.206132	ESTs	lo-hi-lo
	312073	AA682393	"Hs.119237	ESTs	lo-hi-lo
25	312105	T81819	Hs.302251	ESTs	lo-hi-lo
	312108	T82331	"Hs.127453	ESTs	lo-hi-lo
	312292	AW450103	Hs.151124	ESTs	lo-hi-lo
	312313	AW293341	Hs.122505	ESTs, Weakly similar to I38022 hypotheti	lo-hi-lo
	312600	AW970985	Hs.290853	ESTs	lo-hi-lo
30	312800	AI248774	Hs.126707	hypothetical protein FLJ11457	lo-hi-lo
	312821	AA699325	Hs.269880	ESTs	lo-hi-lo
	313097	AI676164	Hs.204339	ESTs	lo-hi-lo
	313166	AI801098	Hs.151500	ESTs	lo-hi-lo
	313179	AA927670	Hs.131704	ESTs	lo-hi-lo
35	313280	AW960454	Hs.222830	ESTs	lo-hi-lo
	313689	AI608910	Hs.193288	ESTs	lo-hi-lo
	314146	AI827237	Hs.282884	ESTs	lo-hi-lo
	314305	AI280112	Hs.125232	Homo sapiens cDNA FLJ13266 fis, clone OV	lo-hi-lo
	314456	AI867931	Hs.164595	ESTs	lo-hi-lo
40	314465	AA602917	Hs.156974	ESTs	lo-hi-lo
	314881	AI095087	Hs.152299	ESTs, Moderately similar to ALU5_HUMAN A	lo-hi-lo
	314916	AA548906	Hs.122244	ESTs	lo-hi-lo
	315043	AA806538	Hs.130732	KIAA1575 protein	lo-hi-lo
	315074	AA828284	Hs.136729	Homo sapiens cDNA: FLJ21348 fis, clone C	lo-hi-lo
45	315214	AI915927	Hs.34771	ESTs	lo-hi-lo
	315344	AW292176	Hs.245834	ESTs	lo-hi-lo
	315353	AI373949	Hs.279610	hypothetical protein FLJ10493	lo-hi-lo
	315439	T78413	Hs.293696	ESTs	lo-hi-lo
	315528	R37257	Hs.184780	ESTs	lo-hi-lo
50	315720	AA292998	Hs.163900	ESTs	lo-hi-lo
	315772	AW515373	Hs.271249	Homo sapiens cDNA FLJ13580 fis, clone PL	lo-hi-lo
	315841	AW136397	Hs.247572	ESTs	lo-hi-lo
	316042	AI469960	Hs.170698	ESTs	lo-hi-lo
	316244	AI640781	Hs.224988	ESTs	lo-hi-lo
55	316345	AW139408	Hs.152940	ESTs	lo-hi-lo
	316625	BE540090	Hs.122156	ESTs	lo-hi-lo
	316738	AA889055	Hs.123468	ESTs	lo-hi-lo
	316868	AI660999	Hs.195602	ESTs	lo-hi-lo
	316905	AW138241	Hs.210846	ESTs	lo-hi-lo
60	317224	X73608	"Hs.93029	sparc/osteonectin, cwcw and kazal-like d	lo-hi-lo
	317275	AI809444	Hs.202108	ESTs	lo-hi-lo
	317404	AI806867	Hs.126594	ESTs	lo-hi-lo
	317488	AW071851	Hs.130628	ESTs	lo-hi-lo
	317916	AI565071	Hs.159983	ESTs	lo-hi-lo
65	317939	AI986209	Hs.244760	ESTs	lo-hi-lo
	318486	T23514		gb:seq3329 1-NIB Homo sapiens cDNA clone	lo-hi-lo
	319897	N46574	Hs.43838	ESTs	lo-hi-lo
	320654	AI160015	Hs.118112	ESTs	lo-hi-lo
	320697	N62937	Hs.269109	ESTs	lo-hi-lo
70	320787	AW088363	Hs.246240	ESTs	lo-hi-lo
	321023	AW294316	Hs.125608	ESTs	lo-hi-lo
	321899	AW972832	Hs.29468	ESTs	lo-hi-lo
	322939	AA101697	Hs.211270	ESTs	lo-hi-lo
	323045	AA148950	Hs.188836	ESTs	lo-hi-lo
75	323091	AI902455	Hs.210761	ESTs	lo-hi-lo
	323262	AL133990	Hs.190642	ESTs	lo-hi-lo
	323410	AW118683	Hs.154150	ESTs	lo-hi-lo
	323645	AW445014	Hs.197746	ESTs	lo-hi-lo
	324598	AW972227	Hs.163986	Homo sapiens cDNA: FLJ22765 fis, clone K	lo-hi-lo
80	324666	T78413	Hs.293696	ESTs	lo-hi-lo
	324674	AA541323	Hs.115831	ESTs	lo-hi-lo
	324713	AI093930	"Hs.313466	ESTs	lo-hi-lo
	324790	AI334367	Hs.159337	ESTs	lo-hi-lo
	324804	AI692552		gb:wd73f12.x1 NCI_CGAP_Lu24 Homo sapiens	lo-hi-lo
	330728	AI905520	Hs.29672	ESTs	lo-hi-lo
	330760	H04588	Hs.30469	ESTs	lo-hi-lo

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5	330776	AW953805	Hs.21887	ESTs	lo-hi-lo
	330824	AB037732	Hs.61441	KIAA1311 protein	lo-hi-lo
	331028	AI539652	Hs.28338	KIAA1546 protein	lo-hi-lo
	331046	N66563	Hs.191358	ESTs	lo-hi-lo
	331050	BE007967	Hs.155795	ESTs	lo-hi-lo
10	331053	AI949841	Hs.183146	ESTs, Moderately similar to ALU1_HUMAN A	lo-hi-lo
	331180	R46692	Hs.6640	Human DNA sequence from PAC 75N13 on chr	lo-hi-lo
	331313	AA761094	*Hs.80618	hypothetical protein	lo-hi-lo
	331337	N74392	Hs.50495	ESTs	lo-hi-lo
	331393	AW976438	*Hs.17428	RBP1-like protein	lo-hi-lo
15	331432	AA282451	Hs.38485	ESTs	lo-hi-lo
	331517	AA765603	Hs.180877	H3 histone, family 3B (H3.3B)	lo-hi-lo
	331686	AW474960	Hs.182258	ESTs	lo-hi-lo
	332002	AI579909	Hs.105104	ESTs	lo-hi-lo
	332043	AA371307	Hs.125056	ESTs	lo-hi-lo
20	332265	AW770320	Hs.222413	ESTs	lo-hi-lo
	332314	R41396	Hs.101774	hypothetical protein FLJ23045	lo-hi-lo
	331517	AB037789	Hs.263395	sema domain, transmembrane domain (TM),	lo-hi-lo
	315352	AA604799	Hs.136528	ESTs, Moderately similar to ALU1_HUMAN A	lo-hi-lo
	315498	AA628539	Hs.116252	ESTs, Moderately similar to ALU1_HUMAN A	lo-hi-lo
25	321489	AI459177	Hs.172759	ESTs, Moderately similar to ALU7_HUMAN A	lo-hi-lo
	106099	NM_012068	Hs.9754	activating transcription factor 5	lo-hi-lo
	105726	NM_012068	Hs.9754	activating transcription factor 5	lo-hi-lo
	319926	AI820719	Hs.154662	DnaJ (Hsp40) homolog, subfamily A, membe	lo-hi-lo
	314915	AI673735	Hs.187748	ESTs, Weakly similar to ALU1_HUMAN ALU S	lo-hi-lo
30	315198	AI741506	Hs.186753	ESTs, Weakly similar to ALU1_HUMAN ALU S	lo-hi-lo
	324302	AW972771	Hs.292471	ESTs, Weakly similar to ALU1_HUMAN ALU S	lo-hi-lo
	331341	BE541042	*Hs.23240	Homo sapiens cDNA FLJ13496 fis, clone PL	lo-hi-lo
	113783	AL359588	Hs.7041	hypothetical protein DKFZp762B226	lo-hi-lo
	313552	AI889208	Hs.17283	hypothetical protein FLJ10890	lo-hi-lo
35	103993	AA315993	Hs.105484	Homo sapiens regenerating gene type IV m	lo-hi-lo
	331492	AK001114	Hs.53913	hypothetical protein FLJ10252	lo-hi-lo
	110837	H03109	Hs.108920	HT018 protein	lo-hi-lo
	330814	AI955040	Hs.265398	ESTs, Weakly similar to transformation-r	lo-hi-lo
	312226	AA315703	Hs.199993	ESTs	lo-hi-lo
40	102034	AI903474	Hs.230	fibromodulin	lo-hi-lo
	134671	BE263255	Hs.302749	FK506-binding protein 9 (63 kD)	lo-hi-lo
	131083	Y09763	Hs.22785	gamma-aminobutyric acid (GABA) A recepto	lo-hi-lo
	309575	AW168096	Hs.169476	glyceraldehyde-3-phosphate dehydrogenase	lo-hi-lo
	134332	D86952	Hs.81875	growth factor receptor-bound protein 10	lo-hi-lo
45	132904	NM_005518	Hs.59889	3-hydroxy-3-methylglutaryl-Coenzyme A sy	lo-hi-lo
	302910	N77976	Hs.251577	hemoglobin, alpha 1	lo-hi-lo
	133731	N71725	*Hs.272572	hemoglobin, alpha 2	lo-hi-lo
	303297	AF070623	Hs.13423	Homo sapiens clone 24468 mRNA sequence	lo-hi-lo
	108732	AA258888	Hs.107476	ATP synthase, H+ transporting, mitochond	lo-hi-lo
50	108731	AA258888	Hs.107476	ATP synthase, H+ transporting, mitochond	lo-hi-lo
	302123	AB013452	Hs.144931	ATPase, aminophospholipid transporter (A	lo-hi-lo
	131614	AB002438	Hs.29586	Homo sapiens mRNA from chromosome 5q21-2	lo-hi-lo
	104933	N94126	Hs.12969	hypothetical protein	lo-hi-lo
	302235	AL049987	Hs.166361	Homo sapiens mRNA; cDNA DKFZp564F112 (fr	lo-hi-lo
55	320574	AL049443	Hs.161283	Homo sapiens mRNA; cDNA DKFZp566N2020 (f	lo-hi-lo
	324578	AI990739	Hs.77868	ORF	lo-hi-lo
	331022	H03109	Hs.108920	HT018 protein	lo-hi-lo
	332430	H25350	Hs.21145	hypothetical protein FLJ22489	lo-hi-lo
	330601	U90916	Hs.82845	Homo sapiens cDNA: FLJ21930 fis, clone H	lo-hi-lo
60	101988	AF221521	Hs.8068	hematopoietic PBX-interacting protein	lo-hi-lo
	102859	AL036058	*Hs.76807	major histocompatibility complex, class	lo-hi-lo
	101363	M11321			lo-hi-lo
	133968	AA355986	Hs.232068	transcription factor 8 (represses interl	lo-hi-lo
	332530	M31669	Hs.1735	inhibin, beta B (activin AB beta polypep	lo-hi-lo
65	317777	NM_014785	Hs.47313	KIAA0258 gene product	lo-hi-lo
	100452	D87742	Hs.241552	KIAA0268 protein	lo-hi-lo
	112988	NM_014867	Hs.5333	KIAA0711 gene product	lo-hi-lo
	320848	AB020691	Hs.198232	KIAA0884 protein	lo-hi-lo
	105152	AL133033	*Hs.4084	KIAA1025 protein	lo-hi-lo
70	133905	AB028974	Hs.137476	KIAA1051 protein	lo-hi-lo
	331406	BE176893	Hs.23440	KIAA1105 protein	lo-hi-lo
	321441	AF107493	Hs.118498	Homo sapiens LUCA-15 protein mRNA, splic	lo-hi-lo
	131913	AW207440	Hs.185973	degenerative spermatocyte (homolog Dros	lo-hi-lo
	135424	U67611		transaldolase 1	lo-hi-lo
75	128506	L40904	Hs.100724	peroxisome proliferative activated recep	lo-hi-lo
	330506	AI130740	Hs.6241	phosphoinositide-3-kinase, regulatory su	lo-hi-lo
	311251	AI655662	Hs.197698	ESTs	lo-hi-lo
	314171	AI821895	Hs.193481	ESTs	lo-hi-lo
	106096	AW379378	Hs.170121	protein tyrosine phosphatase, receptor t	lo-hi-lo
80	133740	AW162919	*Hs.170160	RAB2, member RAS oncogene family-like	lo-hi-lo
	119521	W38038			lo-hi-lo
	119546	W38169			lo-hi-lo
	119559	W38197			lo-hi-lo
	133797	AL133921	Hs.76272	retinoblastoma-binding protein 2	lo-hi-lo
	305096	AA642964	Hs.163593	ribosomal protein L18a	lo-hi-lo
	120256	AA169801	Hs.98710	hypothetical protein	lo-hi-lo

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5	322919	AA178955	Hs.271439	ESTs	lo-hi-lo
	300566	R34926	Hs.326392	son of sevenless (Drosophila) homolog 1	lo-hi-lo
	330694	AI741817	Hs.108447	spinocerebellar ataxia 7 (olivopontocere	lo-hi-lo
	302416	AL120259	Hs.76891	stannin	lo-hi-lo
	319289	AA037634	Hs.79059	transforming growth factor, beta recepto	lo-hi-lo
10	134656	AI750878	Hs.87409	thrombospondin 1	lo-hi-lo
	130117	U06641	Hs.150207	UDP glycosyltransferase 2 family, polype	lo-hi-lo
	124357	N22401		gb:ym37g07.s1 Morton Fetal Cochlea Homo	lo-hi-lo
	108293	AA069155		gb:zm10f1.1.s1 Stratagene pancreas (93720	lo-hi-lo
	108657	BE567753	Hs.132955	BCL2/adenovirus E1B 19kD-interacting pro	lo-hi-lo
15	108658	AA641695		gb:nr62h10.s1 NCI_CGAP_Lym3 Homo sapiens	lo-hi-lo
	331278	AA071383		gb:zm61d05.r1 Stratagene fibroblast (937	lo-hi-lo
	108340	AA069820	Hs.180909	peroxiredoxin 1	lo-hi-lo
	108679	AA115963	Hs.323423	ESTs, Moderately similar to B Chain B,	lo-hi-lo
	108406	AA075424	Hs.325505	ESTs, Moderately similar to HBA_HUMAN HE	lo-hi-lo
20	114598	AA075601		gb:zm89c05.r1 Stratagene ovarian cancer	lo-hi-lo
	108462	AA079347		gb:zm96c06.s1 Stratagene colon HT29 (937	lo-hi-lo
	108466	AA079409		gb:zm96h02.s1 Stratagene colon HT29 (937	lo-hi-lo
	108489	AA082977		gb:zn07h10.r1 Stratagene hNT neuron (937	lo-hi-lo
	330859	AA082977		gb:zn07h10.r1 Stratagene hNT neuron (937	lo-hi-lo
25	108505	AA083376		gb:zn09g08.s1 Stratagene hNT neuron (937	lo-hi-lo
	331283	AA467736	Hs.275437	ESTs	lo-hi-lo
	100641	AW068302	"Hs.182183	Homo sapiens mRNA for caldesmon, 3' UTR	lo-hi-lo-hi
	100642	AW068302	"Hs.182183	Homo sapiens mRNA for caldesmon, 3' UTR	lo-hi-lo-hi
	325889			CH.16_hs gjl5867087	lo-hi-lo-hi
30	338038			CH22_EM:AC005500.GENSCAN.149-9	lo-hi-lo-hi
	338316			CH22_EM:AC005500.GENSCAN.304-2	lo-hi-lo-hi
	100999	H38765	Hs.80706	diaphorase (NADH/NADPH) (cytochrome b-5	lo-hi-lo-hi
	331131	R54797		gb:yg87b07.s1 Soares infant brain 1NIB H	lo-hi-lo-hi
	310955	AI476732	Hs.263912	ESTs	lo-hi-lo-hi
35	311137	AW207582	Hs.196042	ESTs	lo-hi-lo-hi
	311598	AW023595	Hs.232048	ESTs	lo-hi-lo-hi
	313070	AI422023	Hs.161338	ESTs	lo-hi-lo-hi
	110844	AI740792	Hs.167531	methylcrotonoyl-Coenzyme A carboxylase 2	lo-hi-lo-hi
	120328	AA923278	Hs.290905	ESTs, Weakly similar to protease [H.sapi	lo-hi-lo-hi
40	105914	AW245680	Hs.9701	growth arrest and DNA-damage-inducible,	lo-hi-lo-hi
	129389	NM_012445	"Hs.288126	spondin 2, extracellular matrix protein	lo-hi-lo-hi
	102759	NM_005100	Hs.788	A kinase (PRKA) anchor protein (gravin)	lo-lo-hi
	100168	H73444	Hs.394	adrenomedullin	lo-lo-hi
	102348	U37519	Hs.87539	aldehyde dehydrogenase 8	lo-lo-hi
45	134158	U15174	Hs.79428	BCL2/adenovirus E1B 19kD-interacting pro	lo-lo-hi
	133908	AU076820	Hs.325474	caldesmon 1	lo-lo-hi
	101883	AU076743	Hs.75613	CD36 antigen (collagen type I receptor,	lo-lo-hi
	327821			CH.05_hs gjl5867968	lo-lo-hi
	134133	AA262294	Hs.180383	dual specificity phosphatase 6	lo-lo-hi
50	103000	NM_001975	"Hs.146580	enolase 2, (gamma, neuronal)	lo-lo-hi
	109251	AA194776	Hs.85935	EST	lo-lo-hi
	315566	AB037810	Hs.18760	KIAA1389 protein	lo-lo-hi
	324697	AK000742	Hs.126774	L2DTL protein	lo-lo-hi
	306011	AA896986		gb:al06a08.s1 Earstead spleen HPLRB2 Hom	lo-lo-hi
55	307111	AI174528		gb:zan45g10.s1 Gessler Wilms tumor Homo s	lo-lo-hi
	106639	AV655272	Hs.20252	novel Ras family protein	lo-lo-hi
	106753	AI656166	Hs.7331	hypothetical protein FLJ22316	lo-lo-hi
	107974	AW955103	Hs.61712	pyruvate dehydrogenase kinase, isoenzyme	lo-lo-hi
	112033	R49031	Hs.22627	ESTs	lo-lo-hi
60	113816	H46008	Hs.31518	ESTs	lo-lo-hi
	116024	AA088767	"Hs.83883	transmembrane, prostate androgen induced	lo-lo-hi
	116158	AA381807	Hs.61762	hypoxia-inducible protein 2	lo-lo-hi
	119071	R31180		gb:yn62b02.s1 Soares placenta Nb2HP Homo	lo-lo-hi
	120132	W57554	Hs.125019	ESTs	lo-lo-hi
65	120655	AA305599	Hs.238205	hypothetical protein PRO2013	lo-lo-hi
	122411	AW172366	Hs.99083	ESTs	lo-lo-hi
	320779	AA815354	Hs.169898	ESTs	lo-lo-hi
	321024	AW246216	Hs.32058	Homo sapiens C1orf19 mRNA, partial cds	lo-lo-hi
	321408	AW081530	Hs.137088	ESTs, Weakly similar to ALU1_HUMAN ALU S	lo-lo-hi
70	323620	AA306997	Hs.268362	ESTs, Weakly similar to hypothetical pro	lo-lo-hi
	314946	AI097229	Hs.217484	ESTs	lo-lo-hi
	320683	AA334511	Hs.26638	ESTs, Weakly similar to unnamed protein	lo-lo-hi
	128959	AI580127	Hs.107381	hypothetical protein FLJ11200	lo-lo-hi
	128896	T53925	Hs.107	fibrinogen-like 1	lo-lo-hi
75	133592	AV652066	Hs.75113	general transcription factor IIIA	lo-lo-hi
	103245	BE566343	"Hs.28988	glutaredoxin (thioltransferase)	lo-lo-hi
	314785	AI538226	Hs.32976	guanine nucleotide binding protein 4	lo-lo-hi
	103677	Z83806		gb:H.sapiens mRNA for axonemal dynein he	lo-lo-hi
	131170	NM_014253	"Hs.23796	odc (odd Oz/ten-m, Drosophila) homolog 1	lo-lo-hi
80	131164	AW013807	Hs.182265	keratin 19	lo-lo-hi
	100409	D86957	Hs.80712	KIAA0202 protein	lo-lo-hi
	133167	AW162840	Hs.6641	kinesin family member 5C	lo-lo-hi
	319080	AW967646	Hs.23023	ESTs	lo-lo-hi
	330706	AF097994	Hs.301528	L-kynurenine/alpha-aminoadipate aminotra	lo-lo-hi
	104052	NM_002407	Hs.97644	mammaglobin 2	lo-lo-hi
	100647	M57417		gb:Homo sapiens mucin (mucin) mRNA, part	lo-lo-hi

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	103145	X66276	Hs.169849	myosin-binding protein C, slow-type	lo-lo-hi
	301015	AV655272	Hs.20252	novel Ras family protein	lo-lo-hi
	311013	AA224760	"Hs.153	ribosomal protein L7	lo-lo-hi
5	132050	AI267615	Hs.38022	ESTs	lo-lo-hi
	132349	AW975854	"Hs.181286	serine protease inhibitor, Kazal type 1	lo-lo-hi
	130889	AW972512	Hs.20985	sin3-associated polypeptide, 30kD	lo-lo-hi
	130791	AF030403	Hs.199263	Ste-20 related kinase	lo-lo-hi
	130385	AW067800	Hs.155223	stanniocalcin 2	lo-lo-hi
10	127229	AA316181	Hs.61635	six transmembrane epithelial antigen of	lo-lo-hi
	133820	S69681	"Hs.177582	surfactant, pulmonary-associated protein	lo-lo-hi
	129523	M13231	Hs.274509	T cell receptor gamma constant 2	lo-lo-hi
	321415	BE621807	Hs.3337	transmembrane 4 superfamily member 1	lo-lo-hi
	131859	AW960564	"Hs.3337	transmembrane 4 superfamily member 1	lo-lo-hi
15	133444	M63978	Hs.73793	vascular endothelial growth factor	lo-lo-hi
	332567	AW939251	"Hs.25647	v-fos FBJ murine osteosarcoma viral onco	lo-lo-hi
	131328	AW939251	"Hs.25647	v-fos FBJ murine osteosarcoma viral onco	lo-lo-hi
	315901	AI521558	Hs.7331	hypothetical protein FLJ22316	lo-lo-hi
	104394	AA129551	Hs.172129	Homo sapiens cDNA: FLJ21409 fis, clone C	lo-lo-hi
20	103739	AA115173		gb:zn30d02.s1 Stratagene neuroepithelium	lo-lo-hi
	103797	AA080912		gb:zn04d03.r1 Stratagene hNT neuron (937	lo-lo-hi
	103804	AA129196		gb:zn29d08.r1 Stratagene neuroepithelium	lo-lo-hi

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TABLE 1B

Pkey: Unique Eos probeset identifier number
CAT number: Gene cluster number
Accession: Genbank accession numbers

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Pkey	CAT Number	Accessions
108452	116651_1	AA079347 AA079506 AA079538 AA079442
108489	116662_1	AA082977 AA082955 AA082956
101216	17379_1	AA284166 AA314707 L25876 L27711 AA092745 N92087 U02681 AA315766 BE385121 AA352693 NM_005192 AI739135 AI066521 AW173105
		AA257103 AA450169 AW261971 AA305065 AI954494 AW950384 AW732122 AA830348 AA789097 AA777794 AA284072 BE564465 AI005313
		AA804528 AI041134 AI700317 AI352491 AA856987 AA769007 AA494334 AA769862 AA831168 AI143496 BE090796 AA831166 AI141222
		AI372907 N64843 AI075136 AI076701 AA464156 AI076409 AI273523 AA627383 BE043332 T96665 AA158102 AA158059 AW340182
		AA257019 AI206700 AI678081 AA757304 AA055005 AW059834 AL039012
	8509_1	AW939251 NM_005252 AU076596 V01512 V01512 AW579058 AA249247 AI590359 AW510478 AW518282 BE046054 AW874080 AI268596
		AA996237 AI695592 AI244117 AA290764 AA401957 AA505678 AA428304 W74018 W74016 AA040944 AI272071 AA745909 AA520979
		AA019816 AI245094 AW009706 AA662636 AW024264 AI268601 AA932024 AW513222 AW024169 AI659705 AA932525 AA975329 AI567603
		AI895320 AA514238 AA020837 AI823966 AA843677 AA477453 AA496353 AW372625 AV656426 K00650 W96346 N62388 R95977 AA434270
		AI093633 T27639 AW960245 AW681177 R15253 N36936 F07701 AA319315 AA337290 AA284642 AA344052 F05184 AA351062 AA378451
		AW794233 AW884380 N36951 R49879 AB022276 AA300350 AW639435 AW191708 BE220350 AA280404 AA485546 AW794235 AV554223
		AW838891 AA295986 N72823 AA335648 AA371089 AW845414 H63166 R12840 AA379680 AA477579 R13148 H71003 H71015 AA362156
		AW750674 AW845415 AA366924 AW606044 AI570368 R31511 R33906 R33921 AW663022 AW360985 AI207838 AW607239 AI672451
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45	110561	4210_1	
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5	132883	4446_1	AA373314 BE042692 AW135187 AW751673 T30808 T17147 F07527 Z43038 AL110207 N56008 AA235809 AA303946 AA187908 H02145 R82250 R21174 T05429 AA149312 H91287 H47312 T59791 AA327743 AW959920 AA047151 AA042929 W79323 N28243 AW361453 T58658 AI633886 AI825845 AI672514 AI669657 AI917587 AI761837 BE466305 AA042976 AA149242 AW002943 AW6852406 AI434824 W79423 AI025949 AI202452 AI635059 H90378 AI373910 AI860143 AI242990 AA972170 H02146 AW237289 AA702239 AA047290 T17146 AI433847 AI086755 AI071424 AI638095 AW303958 AA703636 H62439 AA971818 AA639538 H62425 AI244773 AW104980 AW016719 N23623 R06163 AA961232 AA974465 AI335830 AI991454 AW592598 AW242938 AI611017 AI810716 AW869345 H67615 AI025948 AI420535 AI799741 F34993 AI489542 BE504982 H47393 AI873145 AA918462 R45954 H67078 R06063 H61439 H58198 H61425 R26497 R33068 AA348031 N36289 AA029108 N44785 W32387 AA085513 H99671 N35592 AW025225 N34379 AA908705 H13386 R13339 W02669 W03164 AA938405 D81339 AA197086 AA348647 W03410 AV647005 AA757887 W73230 W73285 AI809089 AA527333 AI096643 AA861288 AA993061 AL119078 N74451 N74398 AA736438 N35475 AW271207 AA782011 AA630851 AI359176 AA911761 N67481 AA470841 W81567 N24828 AA776157 AI220315 AA719560 W35156 AI911196 AA693790 AI023064 AA700944 AA029998 T32810 AA903560 AA991934 AA197014 AI313007 AI244576 AA701095 T32824 N28424 AI620318 AA610082 AI245085 H06050 N42841 Z19860 Z21076 F16768 AA262294 AU076991 D31396 AI750772 AA159076 BE274766 F12663 R59864 R14494 AA393859 BE242904 AB013382 AB013601 X93920 NM_001946 BE302698 BE277522 AA376048 R56303 AW963843 BE303045 AV647942 AA313210 AV645708 AV658608 AV657088 AV656645 AV658779 AA314475 Z44559 R59865 AA304855 AW991466 F10276 R06817 R10611 W03980 T80992 R10613 BE163098 F05427 F05303 T91529 W72835 AA298800 AW389635 AA308036 AA127907 AW389663 AW894164 F12020 T55624 BE175780 H156652 H24811 T59773 BE166275 AA132053 AW290904 AW647431 AI949528 AA120788 AI185315 AI707683 AW020919 AI192566 BE220784 AI342571 BE221591 AW572844 R56221 AA828935 N73917 AW339578 AW613310 T16061 T17184 AW470946 T80993 BE350535 AW088518 BE250462 AA973609 AI085452 D30852 AI418975 AI092972 AI750773 AA779887 AI472189 AI590360 AI913771 AI418318 AA677348 AA857239 AW820356 AA630374 AI570772 AA148198 AA405450 H24635 R06765 AA669326 D45590 AA159077 AW467788 AA776489 T68899 AA636297 AA618367 BE242383 AI814368 Z38329 AW078669 AI925363 AA535062 AA811335 AI361925 AW276471 AI573117 T91845 AW166964 AW665754 AI860504 AI619683 AI491918 BE349335 AI914906 W72836 BE003237 AA610305 AA768101 H16509 AA973395 AA132157 AW304113 AA976980 AA565289 BE207526 AA455254 AA302518 AA856930 AA344776 AI433775 AA446563 AI245402 AI470568 AI167965 AI2667742 F09667 AI251112 AA919150 AA302216 AA535575 AI470424 F01666 AI282775 BE349349 AW293481 BE2605 T65557 F03626 T25166 AA446688 NM_002407 AF071219 AA297452 AA297456 AJ224173 AA297402 AA297405 AW966513 AW966509 AW510561 AA297482 AW451131 AA393164 AI800231 BE044895 BE044893 AI936084 AI491987 AI659370 AW779377 AA398560 AA493295 AW243774 AA298750 AI937042 AA525178 AW207696
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25			AU077115 NM_005778 AF091263 AA558755 AF103802 BE254911 U23946 AA300552 AA300658 AW366740 U73168 BE168234 AW071451 F12188 AI082769 BE304364 Z44416 T64836 AI360219 T99027 AA053236 AA287188 AA705726 AA677451 R21564 W76177 T10051 W73892 AW805335 AW803972 AW935657 AW618294 AW582571 AW858746 AW862020 R37062 AW818366 AW936675 AW949579 AA349791 AA337186 AA369780 AI424264 R45829 Z19624 BE386598 BE391503 AW370456 AI907719 AA593262 AA165466 BE184217 AW884123 AA437179 AA249486 AA367141 AA150682 AI719148 AW662385 AI676082 AI336755 AL044121 AI874249 AW080371 AI783726 AW087565 AI351171 AA746150 AI016061 AW862035 AW858817 AI140331 AI831099 AI147008 AI049957 AW182561 AW131871 AA421795 AW103460 AI160679 AA192645 AA773506 AI760715 AA382385 AA869659 AI184657 AI352518 AA570533 AI688574 AW023887 AW473505 N23866 AI689425 AA194028 AW001950 N41616 AI377067 AA699426 AA782487 AI192743 AI140138 AW469862 N29616 AW572110 AA767408 AA192891 AI378243 AI969394 AI923316 AI248994 BE221340 AI076411 AW004939 AA907700 AI247959 AI367846 AW79860 T03540 D19618 AW193738 AI274002 AA724105 AA907774 AA646939 AA904276 AI225052 R45218 AW614769 AI066090 AI417666 AA677951 AA566007 F09819 AA961715 AW149264 AW078952 AI750024 AA659691 AA150773 T31362 AW510627 Z40342 T10050 AA670261 AA563802 T33106 R42942 AA994060 AW512057 AA877988 AI198734 AI653943 AI217242 AI127650 R60960 AI539540 AA782825 AA953465 AW074329 AI701674 AW874346 AA917711 T32698 BE221007 AI125018 AA194215 AW378414 AW378418
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75	122411 121847	300118_1 289808_1	BE545072 AI540751 AA301103 AI916675 N85422 BE563965 AA327978 AI816094 AK001515 BE501319 AA279943 BE138895 AA343765 AW963051 AW082308 AI823992 AI553752 AI599007 AI816135 AI565536 BE501307 AW272765 AW242239 AA766315 AI014927 AA578848 AI354483 AI476548 AI038579 AA973322 AA992180 AW472921 BE504789 AI392988 AA506076 AA769228 AI370562 AL137710 BE005656 AW965920
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5	114660	685_8	AA071383 AA071369 AA083800 AA075976 AA116006 AA075667 AA085142 AA085087 AA076496 AA129187 AA122171 AA076367 AA074080 AA085088 AA084663 AA085094 AA112092 AA075668 AA122253 AA122199 AA071140
	107480	13160_1	AF001691 NM_002705 AF013717 AF041004 AB011140 AW379129 BE149649 AW378873 BE168169 AW084902 AA233948 AA158208 T16869 AW372235 AA507188 AA776617 AW379469 AW372236 AW601186 AW991416 BE184815 AW532622 BE184812 BE184811 AW991619 AW991497 AA025674 AW368139 T57706 AW991434 AW749668 AW576740 AW373236 A1681156 AW749667 AW576752 AW576743 AW991422 AW991557 AW577300 AW577322 AW577319 T57667 AA888121 A1703487 AA025675 T29988 A1298486 W58384 A1680568 W58057 A149765 A1719398 AW991633 AW991569 AW795578 AA632719 D11970 AW265400 A1914109 AA493846 AA233963 A1139713 A1157557 AW749662 T31016 AA099832 A1401181 AA586911
	106849	7043_1	AL137281 BE205870 A1650975 R14487 AA922570 H11891 H29488 H29523 A1206294 A1215425 R38943 R38942 H08943 AA442674 AA306295 AW958068 AW972543 Z19328 A1863078 C02207 BE350493 AA505869 R40812 T93149 H95001 C18110 AA485465 F27445 A143831 AA557309 A137747 BE467304 A1139368 BE348511 F20210 AA912949 AW513418 BE327136 A1127681 A1658928 AA587053 T93063 F33088 A1922245 AA971641 AA663936 AW303901 A1537689 A1283036 A1283962 AW510432 AA708783 H08860 A1363857 AA829264 AA507719 AA829344 A1420107 A1283037 Z19327 F23412 A1678514 F30637 A1864155 AA917438 A1439337 AA485308
	129726	6269_1	H15474 R52848 AF035284 F07283 F13380 R12156 T77191 R13138 R96295 AA356763 AW675367 AA343586 AA489509 AW500426 AF009758 AW341341 A1681262 BE252566 BE252163 AA069088 AA010227 AA307348 H66237 AF009757 AA084193 AA083946 AA374100 AW893308 N36736 AA319191 W76142 AW960664 N31425 AA057653 H10662 BE393342 W81053 AA126186 BE392323 AW902076 F12173 T66054 BE255347 BE251382 AA600210 BE393809 H15419 A114741 BE391404 BE389714 AA057699 AW305118 BE388163 T89453 AW576394 R66422 AF009755 AA489510 H51753 A1497773 W80802 AA778129 AA069023 R52814 AA356586 AW95989 T97693 A1087020 A1732954 R40619 AA633539 R98686 R82699 A1142743 A1038185 H79526 H70618 W72916 R10913 AA704737 AA70104 AW674760 AA011433 AA703446 AA704480 R15088 F03555 AL041978 AA173042 W92755 AA083606 N28538 A1565712 H97486 A1912320 A1027627 AA948084 A1052027 AA432026 A1479405 AW513386 AA630798 AA633546 AA148694 AW130360 AA236623 N22673 AA431773 T55295 AA1226080 A1094889 N24124 W92731 A1380076 A1384060 AW130366 N30429 AA112061 AA236599 AA642566 N26096 BE222996 A1028790 AF009756 AA148695 A1356127 AA083858 W86036 A1311581 AA775310 A1239724 AA992636 AA302659 H08702 AA083963 A1240047 H10663 A1066494 AA468663 T74198 T89542 H79525 AA011652 AA314276 T97793 R82956 T78297 R10967 AA057613 BE185536 AW387821 AA581144 T10391 A1690802 AA345198 AW136974 A1275804 A1348576 A1868133 AA112069 AA487561 AW044496 AA346366 AW272367 T54856 AV652054
	100202	19610_1	BE294407 AL135112 D25328 AA088354 BE273722 BE272668 BE276672 BE514674 BE279911 BE279913 AW239137 H30835 H30695 H39126 AW603879 AA297040 AA853405 AA143274 AA324224 AA102159 BE410931 AA156346 AA143737 T12211 AW178885 W52954 H19449 D21863 AW603830 R47802 R47796 R12860 AW249362 AL121190 AW875029 BE408786 AA374051 BE311615 AA315845 M64784 AA079444 BE076586 AA316113 AA374646 AA324565 AA044376 AA308362 AW951725 AW805242 AA608558 AA384565 A1719345 AW994518 AW891548 A1565573 H30766 H43768 A1813652 AA169712 AW368192 W07368 A187907 AA247371 A1479642 BE300944 AA946886 AA617959 H39092 AA725570 AA570091 AA603074 A1073609 AW864812 A1498239 A1570920 AW769140 AW300823 AW613145 AA227722 AW383865 AA634394 A1568954 A186816 AA622467 AA622586 AW571827 AW517726 W35243 A1653786 A1861994 H28131 A1312567 A1913029 AA565609 AW674259 AW106540 AW103808 AA579837 AA827484 A1199670 A1021785 BE536802 R39433 AA503834 AA878031 A1183668 A1539684 AW770004 AA903232 AA847671 AA617688 AA383688 AA383687 AW248638 A1479052 AW469070 A1634941 AA633506 A1192072 AA873200 A1899874 AA121991 A1070457 A1932686 AA984658 AA406517 AA995260 AA406495 AA769419 A1929848 AA406340 AW512235 A1673540 AA406382 AA284665 A1032219 R87480 A1140638 A1653882 N80241 T28549 N90878 AA826472 A1670799 AW069643 AA169166 A1969266 AA199606 AA156311 A1332993 AA223736 AA847238 AA228101 AA079349 W06432 R49552 AW474675 H28156 H28157 AA303532 A1926938 A1370126 H43690 AA834352 AA648144 AA609613 AA730591 A1274501 AW083391 A1309947 A4740393 AA280414 AW191933 A1015853 A134423 A1367848 AA349442 AA535249 AW009189 AW000717 AA303169 AA543033 A1043513 A1069071 A1038914 AA143275 AA304073 AA688012 T23544 AA923652 AA187749 AA381201 BE122669 AA850553 AA074435 W23575 AA069978 AA143708 AA515680 A1695525 AA044444 BE387839 BE581618 BE535741 BE252119 A1045356 AW572190 H14937 BE36379 W16562 AA554183 BE275809 AW385196 U91917 AA912272 AA988289 N88262 AA187748 AW516465 A1674256 D57241 BE171390 A46258 AA173149 AA206272 AW406375 AA210826 AA324212 A1075920 AW952891 AW070942 A1026835 AW367242 AW602275 AW367332 A1915314 AW104080 AW013923 AW367328 AA287338 AA133979 AL135396 AW978864 AA934545 AA504314 A1363056 A1630392 A1630319 R23055 AA205833 AW673513 AA173276 AA287324 A1004681 AA829651 AA210721 A1376711 AA688155 A1858354 AA126774 AA836121 AA489233 AA598962 R22949 A1026140 A1028632 AA342411 AA599018 R78445 AW593702 AA831728 AW268252 A1343050 BE047778 AA628867
50	100235	6535_1	D29954 AW810400 N86381 T27145 AF070553 R24816 H10674 H05886 T81290 BE081440 AA347340 AW502865 W38633 BE081508 BE545197 N78187 AA354376 AW403884 AW949291 AA430545 N94238 A1827148 AA399070 A1796581 A1684155 T29848 AW949662 AW469201 W44737 R40401 AW469198 AW664344 AW192708 H10675 AW615130 A1862188 N59634 A1292183 A1091968 H90637 H42430 A1033530 H30425 A1291384 AA430546 R45548 A1274765 AA412170 AA574218 R38945 AA773459 R38811 H05779 H42859 BE018564 A1040602 AW505246 AA507084 R13015 AW503464 BE245313 T80046 H44409 AW602308 BE245345 AA536210 X07730 AA859438 M24543 X05332 NM_001648 S75756 U17040 A1525089 A1524893 A1524861 A1646857 A1525128 M26663 A1547285 A1525832 X14810 M27274 A1557591 M21895 AW973948 AW451486 A1547084 AA659534 A639308 AA6534235 A1526979 AA579039 AA225115 AA658261 AA640352 AA229599 AA574023 AA573727 AA535453 AA522842 AA57697 AA659319 AA397360 AA654636 AA653755 AA808858 AA356185 A1826164 AA228945 AA259192 AA228999 T29521 AA557838 A1547051 AA622817 AA397452 A1396076 A1826504 AA577955 AA659391 AA650205 AA640736 AA640280 AA640372 AW957256 AA642495 AA579134 AA523902 AA631704 AA228884 A1524856 A1524842 AA657389 AA572896 AA658494 AA569580 AA640510 AA650269 AW083359 AA654754 AA420678 AA569445 AA654896 A1399713 AA572787 AA662137 A1546893 AA595295 AA216409 AA595094 AA572731 A1669143 AA594993 AA658304 AA622211 AA594942 AA613267 AA622228 AA622221 AA640290 AA541668 AA613665 AA570587 AA420806 AA594947 AA631696 AA579361 AA541677 AA244158 AA244159 AA557834 AA225529 AA564089 AA612574 AA513226 AA568528 AA658266 A1524918 AA420532 AA622386 AA742853 AA622399 AA420427 AA614195 AA177118 AA228440 AA229488 AA225114 AA542918 AA602936 AA595415 AA688100 AA654204 AA533337 AA467972 AA573548 AA650351 AA579038 AW969995 AA659194 AA573563 AA630816 AA654970 AA579480 AA658400 AA226667 AA225626 AA531322 AA229759 AA558395 AA525076 AA420783 AA225043 AA650228 AA420818 AA229219 AA226150 AA658911 AA568333 AA420816 AA513597 AA525050 AA579470 AA226161 AA226222 AA602211 AA527907 AA533137 AA230250 AA641190 AA657860 AA687931 AA397400 AA558678 AA467971 AA573729 AA532918 AA229144 AA569723 AA552572 AA809594 AA531371 AA528279 AA603973 AA533547 AA564296 AA650166 AA550396 AA525122 AA640642 AA639894 AA658551 AA531355 AA654373 AA614206 AA569669 AA244246 AA225154 AA604036 AA548289 AA603549 AA527943 AA524601 AA976367 AA657942 AA602158 AA640996 AA535294 AA603978 AA640517 AA554876 AA524889 AA566020 AA564525 A1734071 AA654743 AA225137 AA603981 AA230145 AA659430 AA605005 AA225509 AA602959 AA564506 AA613839 AA653917 AA603284 AA226430 AA225508 AA530919 AA542887 AA642067 AA653961 AA573590 AA524594 A1535889 AA535572 AA687218 AA243984 AA595609 AA534155 AA650133 AA259191 AA886140 AA228722 AA467814 AA578915 AA551615 A1547277 AA657764 AA894884 AA551616 AA522859 AA572918 AA229957 AA229751 AA531199 AA652522 AA229967 AA551461 AA532935 AA601934 AA230032 AA640714 AA535828 A1865511 AA468362 AA226298 AA659419 AA224930 AA652490 AA573554 AA935415 AA876596 AA550775 AA578325 AA607271 AA640881 AA602193 AA470345 AA470329 AA228299 AA659390 AA503922 AA548920 AA631828 AA468363 AA602725 AA588252 AA937840 AA551700 AA504059 AA640677 AA467991 AA687575 AA569519 AA468448 AA533935 AA230163 AA224955 AA599996 AA573534 AA613750 AA659184 AA468034 AA492276 AA533118 AA177132 AA578322 AA229623 AA578410 AA614248 AA604850 AA602011 AA534015 A1867619 AA535585 AA613770 AA557916 AA641178 AA578039 AA573994 AA468942 AA579411 AA657805 AA886046 AA652492 AA516525 AA652252 AA614074 AA467767 AA469019 AA886501 AA226264 AA224856 AA594919 AA559921 AA224855 AA602123 AA469434 AA574905 AA876824 AA573705 AA657775 AA633434 AA622818 AA580256 AA659550 AA687992 AA468140 AA579217 AA470332 AA468160 AA468372 AA555233 AA935098 AA468122 AA551711 AA641183 AA229801 AA224940 AA570202 AA504034 AA468041 AA228397 AA503262 AA535502 AA886623 AA259272
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	328164	c_6_hs
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	335753	CH22_3120FG_604_2_LINK_EM
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	335756	CH22_3123FG_604_5_LINK_EM
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AW974523 AW195611 AI393315 AI738792 AW665895 AW574679 AA913471 AA651780 AA737663 AI015407 AI366737 AI285359 BE245537
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D58108 AW021706 D57449 D57041 D58277 D56935 AI356974 D57023 AA018712 H27631 D57851 D57514 D57268 D57468 AW805646
AI278945 D57323 D56986 D57539 D57829 D58078 AW805515 AI348684 D57772 R74449 BE041558 D56746 AW798485 D56640 AA985597
D56702 D56849 D56874 AW581419 AA470397 D57591 AW799884 T27640 N68497 D56803 AA618186 AW805647 D57945 N23726 D56637
N23730 D56992 BE176882 BE176838 BE176909 D56757 N68137 D56987 AI559806 AA631437 D57454 D56718 C17030 T29278 D57377

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5	332577	89088_2	AW021936 AW118330 AA515358 D56610 AA494092 D56934 T97774 AI473546 R74350 R84834 AA579200 D56616 C03207 D57391 N52416 D56928 R79209 D56925 AA020879 D45546 AI858769 R20750 T09381 F01435 AW627906 D58202 AI933993 F01912 H27552 AA174191 T16515 AW023216 AA434146 H83387 AI346751 V01512 V01512 AA576407 AW365140 AA937471 BE174681 AI568829 AI274663 R85530 AL048225 H83388 AW798734
10	332640	4172_1	AI826268 AW248872 H69511 AI748806 AW779557 AI992254 AI890377 AW151271 AI356374 AI634503 AA777065 AI590131 H37767 AI889058 H69512 AA046480 N27343 AI573008 AW130925 AI635838 AW594603 AW000790 AI208239 AI275835 AW090294 AA021587 AW273456 AA505726 AW469424 AI400222 AI025723 BE046146 AI128668 BE350462 AW302601 AI299977 AA284809 AI640358 AW470364 AI241794 AA650048 AW090027 H15377 AW615318 D60021 AI934336 AW118536 AI041281 AA614238 R85918 AW571741 AW516692 AW572232 AW515188 AI798585 AI392825 Z40518 AI859580 AA469975 AI537819 AI810684 AI701744 AI370410 BE383083 Z44676 BE002481 BE002532 AA456765 N44196 D60022 C14604 AA021099 AA284872 BE266647 AW249292
15			BE568452 BE297396 AA449593 AW732490 AW069736 BE548667 AA207229 AF044588 NM_003981 BE268994 AW444578 AA471151 BE250747 AW732555 AA074582 BE336856 AW408764 AA191159 BE092129 AA310614 AW958677 AA312276 AW750027 AW750046 AW750032 AW750024 AA188893 AW750054 AW408409 AW750030 BE151875 AA478509 N58721 AA195614 H70079 H75580 BE250401 AA454518 AA007263 AA626405 AA417152 AA004230 AA557354 AW863151 AW863181 AA702179 AI924143 AI671185 BE006198 AA190630 AI638795 AI609113 AI056239 BE537023 BE464668 AA634413 BE208066 BE208833 AW250803 AI337375 AA478510 BE501624 AI814763 AW594726 AI091408 AA827285 AA189108 AW594169 BE618589 BE618040 AL135398 AA632206 AI080126 AI638180 AA725439 AI379107 AI288872 H14801 AI679151 AI263619 AI569213 AI679722 W93249 AA552345 AA417030 AI969543 AA534494 AI038181 AA766364 AA573241 AI754325 AW043937 BE207865 AI291838 N73585 N73539 AW805051 AA808510 AI699813 AW166044 AW104716 H05808 AA248270 BE538022 N56013 AA621586 AA149737 D19671 AW192890 N54283 H73339 AA910989 BE273424 BE560082 AW959012 AA313552
20	332732	5436_1	AW750034 BE072537 BE297947 AW732361 AA449336 D29574 AF191019 NM_015516 BE546494 AL110276 R13844 BE313586 BE336912 R18704 R18703 AA045868 T70952 BE336901 T60387 BE149749 BE271848 BE271902 AA489929 Z45402 T64360 AA305745 AA009451 T95706 H14907 AA299901 C03221 T72431 AW471185 AA335297 AI269100 AA345072 AW965160 H27581 R48910 H25380 AA335281 AW973283 T79590 AW183447 T64172 AI744097 AI342358 AA336102 AA335299 BE208375 AI140834 AA088181 AI860314 AI738613 T70902 R42077 AI884568 AA489798 AI130828 AA009735 H25381 AW612425 R48801 H27507 H30105 H44671 AI631362 AA558470 AW014412 AA552059 AA045801 AW589435 AI039657 H14614 AA974256 R42078 AI245758 T61886 AI559202 AI074139 AI817313 AI041484 AA437138 AI613032 AI147891 AI457945 AW197727 AI074399 AI758636 AI598048 AA972077 M85390 R36989 R71936 AI867492 T40081 Z41115 AA772775 T41013 AI695691 T40996 AI826822 N93464 AW955524 AA088651
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TABLE 1C

Pkey: Unique number corresponding to an Eos probeset

Ref: Sequence source. The 7 digit numbers in this column are Genbank Identifier (GI) numbers. "Dunham I. et al." refers to the publication entitled "The DNA sequence of human chromosome 22." Dunham I. et al. (1999) *Nature* 402:489-495.

Strand: Indicates DNA strand from which exons were predicted.

NL_position: Indicates nucleotide positions of predicted exons.

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10	Pkey	Ref	Strand	NL_position
	332792	Dunham, I. et.al.	Plus	73381-73768
	333135	Dunham, I. et.al.	Plus	3361208-3361369
	333137	Dunham, I. et.al.	Plus	3367643-3367726
	333138	Dunham, I. et.al.	Plus	3369205-3369323
	333139	Dunham, I. et.al.	Plus	3369495-3369571
15	333516	Dunham, I. et.al.	Plus	5570204-5570390
	333517	Dunham, I. et.al.	Plus	5570729-5570925
	333795	Dunham, I. et.al.	Plus	7807688-7807795
	333796	Dunham, I. et.al.	Plus	7808253-7808319
	333808	Dunham, I. et.al.	Plus	7880600-7880775
20	333809	Dunham, I. et.al.	Plus	7880600-7880775
	333845	Dunham, I. et.al.	Plus	8005832-8005945
	333849	Dunham, I. et.al.	Plus	8018323-8018472
	334101	Dunham, I. et.al.	Plus	9973413-9973550
	334616	Dunham, I. et.al.	Plus	15176123-15176470
25	334891	Dunham, I. et.al.	Plus	19299770-19299944
	334899	Dunham, I. et.al.	Plus	19315168-19315311
	334900	Dunham, I. et.al.	Plus	19315578-19315743
	334902	Dunham, I. et.al.	Plus	19317083-19317195
	334905	Dunham, I. et.al.	Plus	19322553-19322680
30	334906	Dunham, I. et.al.	Plus	19323493-19323590
	335044	Dunham, I. et.al.	Plus	20842088-20842682
	335149	Dunham, I. et.al.	Plus	21497441-21497587
	335809	Dunham, I. et.al.	Plus	26310772-26310909
	335810	Dunham, I. et.al.	Plus	26314767-26314849
35	335824	Dunham, I. et.al.	Plus	26376860-26376942
	336054	Dunham, I. et.al.	Plus	29161685-29161937
	336721	Dunham, I. et.al.	Plus	3371522-3371586
	337182	Dunham, I. et.al.	Plus	23934889-23934962
40	337674	Dunham, I. et.al.	Plus	3332616-3332697
	337675	Dunham, I. et.al.	Plus	3335368-3335505
	337755	Dunham, I. et.al.	Plus	3971764-3971900
	338038	Dunham, I. et.al.	Plus	8138219-8138392
	338316	Dunham, I. et.al.	Plus	17089711-17089988
45	333124	Dunham, I. et.al.	Minus	3318017-3317932
	333743	Dunham, I. et.al.	Minus	7573218-7573060
	334221	Dunham, I. et.al.	Minus	12730944-12730387
	334222	Dunham, I. et.al.	Minus	12732417-12732289
	334282	Dunham, I. et.al.	Minus	13285293-13285178
50	334502	Dunham, I. et.al.	Minus	14488605-14488626
	334578	Dunham, I. et.al.	Minus	15004462-15004304
	334951	Dunham, I. et.al.	Minus	20147708-20147502
	335289	Dunham, I. et.al.	Minus	22305950-22305708
	335290	Dunham, I. et.al.	Minus	22309950-22309891
	335293	Dunham, I. et.al.	Minus	22316408-22316275
55	335682	Dunham, I. et.al.	Minus	25421215-25421093
	335753	Dunham, I. et.al.	Minus	25761535-25761444
	335755	Dunham, I. et.al.	Minus	25763806-25763747
	335756	Dunham, I. et.al.	Minus	25764330-25764251
	336662	Dunham, I. et.al.	Minus	2158060-2157993
60	336684	Dunham, I. et.al.	Minus	2158060-2157993
	337603	Dunham, I. et.al.	Minus	1299296-1299194
	338561	Dunham, I. et.al.	Minus	22311966-22311856
	338562	Dunham, I. et.al.	Minus	22312594-22312465
	339186	Dunham, I. et.al.	Minus	32339211-32339097
65	325889	5867087	Plus	223829-223891
	330032	6682596	Plus	85177-85237
	330033	6682596	Plus	86663-86723
	326213	5867224	Minus	60751-60927
	326816	6552458	Plus	198354-198436
70	327110	6117842	Plus	94608-94785
	327821	5867968	Plus	131060-131232
	328164	5868068	Minus	27080-27226
	328648	6004473	Plus	424829-424959
75	329365	5868838	Minus	107687-107765

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Pattern: Broadly defined expression patterns during androgen withdrawal

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	441328	AI982794	Hs.159473	ESTs	lo-lo-hi-lo
	416508	R39769		ESTs, Moderately similar to ALU8_HUMAN A	lo-lo-hi-lo
	451066	AI758660	Hs.206132	ESTs	lo-lo-hi-lo
5	446017	N98238	Hs.55185	ESTs	lo-lo-hi-lo
	447104	R19085	Hs.210706	Homo sapiens cDNA FLJ13182 fis, clone NT	lo-lo-hi-lo
	447211	AL161961	Hs.17767	KIAA1554 protein	lo-lo-hi-lo
	447765	AW014112	Hs.161390	ESTs	lo-lo-hi-lo
	429540	M85776		gb:EST02297 Fetal brain, Stratogene (cat	lo-lo-hi-lo
10	444314	AI140497		gb:ow76b09.s1 Soares_fetal_liver_spleen_	lo-lo-hi-lo
	414555	N98569	Hs.76422	phospholipase A2, group IIA (platelets,	lo-lo-hi-lo
	432677	NM_004482	Hs.278611	UDP-N-acetyl-alpha-D-galactosamine:polyp	lo-lo-hi-lo
	422091	AI906339	Hs.97927	ESTs	lo-lo-hi-lo
	423028	H90946		gb:yu86c02.r1 Soares fetal liver spleen	lo-lo-hi-lo
	444040	AF204231	Hs.182982	golgin-67	lo-lo-hi-lo
15	441111	AI806867	Hs.126594	ESTs	lo-lo-hi-lo
	418838	AW385224	Hs.35198	ectonucleotide pyrophosphatase/phosphodi	lo-lo-hi-lo
	415999	AA172179	Hs.294029	ESTs	lo-lo-hi-lo
	429615	AF258627	Hs.211562	ATP-binding cassette, sub-family A (ABC1	lo-lo-hi-lo
20	427774	AA278583	Hs.180737	Homo sapiens clone 23664 and 23905 mRNA	lo-lo-hi-lo
	438585	AA811371	Hs.123362	ESTs	lo-lo-hi-lo
	424776	AI867931	Hs.164595	ESTs	lo-lo-hi-lo
	413786	AW613780	Hs.13500	ESTs	lo-lo-hi-lo
	421077	AK000061	Hs.101590	hypothetical protein	lo-lo-hi-lo
	445837	AI261700	Hs.145544	ESTs	lo-lo-hi-lo
25	449282	ALD48056	Hs.23437	Homo sapiens cDNA FLJ13555 fis, clone PL	lo-lo-hi-lo
	414065	AW515373	Hs.271249	Homo sapiens cDNA FLJ13580 fis, clone PL	lo-lo-hi-lo
	432527	AW975028	Hs.102754	ESTs	lo-lo-hi-lo
	412093	BE242691	Hs.14947	ESTs	lo-lo-hi-lo
30	457121	AI743770	Hs.180513	ESTs, Weakly similar to KIAA0822 protein	lo-lo-hi-lo
	417280	AW173116	Hs.250103	ESTs	lo-lo-hi-lo
	452445	AB002438	Hs.29596	Homo sapiens mRNA from chromosome 5q21-2	lo-lo-hi-lo
	438624	AA889055	Hs.123468	ESTs	lo-lo-hi-lo
	442343	AA992480	Hs.129874	ESTs	lo-lo-hi-lo
35	401416			C14000338:gij7459502 pir S74665 outer	lo-lo-hi-lo
	437176	AW176909	Hs.42346	calcineurin-binding protein calcardin-1	lo-lo-hi-lo
	451663	AI872360	Hs.209293	ESTs	lo-lo-hi-lo
	449295	AW137268	Hs.270954	ESTs	lo-lo-hi-lo
	426848	H72531	Hs.36190	ESTs	lo-lo-hi-lo
40	445467	AI239832	Hs.15617	ESTs, Weakly similar to ALU4_HUMAN ALU S	lo-lo-hi-lo
	418662	AI601098	Hs.151500	ESTs	lo-lo-hi-lo
	416239	AL039450	Hs.48948	ESTs	lo-lo-hi-lo
	428054	AI948688	Hs.266619	ESTs	lo-lo-hi-lo
	435284	AA879470	Hs.96849	Homo sapiens cDNA FLJ11492 fis, clone HE	lo-lo-hi-lo
45	424332	AA338919	Hs.101615	ESTs	lo-lo-hi-lo
	442369	AI565071	Hs.159983	ESTs	lo-lo-hi-lo
	420717	AA294447	Hs.271887	ESTs	lo-lo-hi-lo
	439684	AA838114	Hs.221612	ESTs	lo-lo-hi-lo
	440260	AI972867	Hs.7130	copine IV	lo-lo-hi-lo
50	426269	HI5302	Hs.168950	Homo sapiens mRNA; cDNA DKFZp566A1046 (f	lo-lo-hi-lo
	428398	AI249368	Hs.98558	ESTs	lo-lo-hi-lo
	407276	AI951118	Hs.326736	Homo sapiens breast cancer antigen NY-BR	lo-lo-hi-lo
	409339	AB020666	Hs.54037	ectonucleotide pyrophosphatase/phosphodi	lo-lo-hi-lo
	442150	AI368158	Hs.70983	PTPL1-associated RhoGAP 1	lo-lo-hi-lo
55	415787	H01463	Hs.93534	ESTs	lo-lo-hi-lo
	430685	AI690234	Hs.191666	ESTs, Weakly similar to GNMSLL retroviri	lo-lo-hi-lo
	443794	N94104	Hs.29280	ESTs	lo-lo-hi-lo
	446215	AW821329	Hs.14368	SH3 domain binding glutamic acid-rich pr	lo-lo-hi-lo
	441285	NM_002374	Hs.167	microtubule-associated protein 2	lo-lo-hi-lo
60	448738	BE614081		gb:601503816F1 NIH_MGC_71 Homo sapiens c	lo-lo-hi-lo
	403746			ENSP00000226812:KIAA1494 protein (Fragm	lo-lo-hi-lo
	434022	R18374	Hs.117956	ESTs	lo-lo-hi-lo
	435714	AA699326	Hs.269880	ESTs	lo-lo-hi-lo
	439848	AW979249		gb:EST391359 MAGE resequences, MAGP Homo	lo-lo-hi-lo
65	421974	AA301270		gb:EST14192 Testis tumor Homo sapiens cD	lo-lo-hi-lo
	433332	AI367347	Hs.44889	Homo sapiens clone TCCCTA00151 mRNA sequ	lo-lo-hi-lo
	449919	AI674685	Hs.200141	ESTs	lo-lo-hi-lo
	407192	AA609200		gb:af12e02.s1 Soares_testis_NHT Homo sap	lo-lo-hi-lo
	436169	AA886311	Hs.17602	Homo sapiens cDNA FLJ12381 fis, clone MA	lo-lo-hi-lo
70	418624	AI734080	Hs.104211	ESTs	lo-lo-hi-lo
	432432	AA541323	Hs.115831	ESTs	lo-lo-hi-lo
	426172	AA371307	Hs.125056	ESTs	lo-lo-hi-lo
	401093			C12000586:gij6330167 dbj EAA86477.1 (A	lo-lo-hi-lo
	426716	NM_006379	Hs.171921	sema domain, immunoglobulin domain (Ig),	lo-lo-hi-lo
75	439569	AW602166	Hs.222399	CEGP1 protein	lo-lo-hi-lo
	451720	AW970985	Hs.290853	ESTs	lo-lo-hi-lo
	429163	AA884766		gb:am20e10.s1 Soares_NFL_T_GBC_S1 Homo s	lo-lo-hi-lo
	432435	BE218886	Hs.282070	ESTs	lo-lo-hi-lo
	406170	AW204516	Hs.31835	ESTs	lo-lo-hi-lo
80	433530	BE349534	Hs.281789	ESTs	lo-lo-hi-lo
	425776	U25128	Hs.159499	parathyroid hormone receptor 2	lo-lo-hi-lo
	430068	AA464964		gb:zx80f10.s1 Soares_ovary tumor NbHOT H	lo-lo-hi-lo
	422725	AA315703	Hs.199993	ESTs, Weakly similar to ALUB_HUMAN !!!	lo-lo-hi-lo

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5	432314	AA533447	Hs.312989	ESTs	lo-lo-hi-lo
	434609	R76593		gb:y160c11.r1 Soares placenta Nb2HP Homo	lo-lo-hi-lo
	448760	AA313825	Hs.21941	AD036 protein	lo-lo-hi-lo
	417381	AF164142	Hs.82042	solute carrier family 23 (nucleobase tra	lo-lo-hi-lo
	456334	T50392	Hs.271745	ESTs	lo-lo-hi-lo
10	435445	AA737345	Hs.294041	ESTs	lo-lo-hi-lo
	411928	AA888624	Hs.197289	rab3 GTPase-activating protein, non-cata	lo-lo-hi-lo
	438869	AF075009		gb:Homo sapiens full length insert cDNA	lo-lo-hi-lo
	423932	T95633	Hs.189703	ESTs	lo-lo-hi-lo
	422222	AI699372	Hs.193247	hypothetical protein DKFZp434A171	lo-lo-hi-lo
15	434941	AW073202	Hs.334825	Homo sapiens cDNA FLJ14752 fis, clone NT	lo-lo-hi-lo
	415736	AA827082	Hs.291872	ESTs	lo-lo-hi-lo
	432722	AA830532	Hs.326150	ESTs	lo-lo-hi-lo
	435511	AA683336	Hs.189045	ESTs	lo-lo-hi-lo
	432242	AW022715	Hs.162160	ESTs, Weakly similar to ALU4_HUMAN ALU S	lo-lo-hi-lo
20	451141	AW772713	Hs.247186	ESTs	lo-lo-hi-lo
	450546	AA010200	Hs.175551	ESTs	lo-lo-hi-lo
	413351	BE086815		ESTs	lo-lo-hi-lo
	439324	AF086134	Hs.94309	ESTs	lo-lo-hi-lo
	452688	AA721140	Hs.49930	ESTs, Weakly similar to putative p150 [H	lo-lo-hi-lo
25	415669	NM_005025	Hs.78589	serine (or cysteine) proteinase inhibitor	lo-lo-hi-lo
	450164	AI239923	Hs.63931	ESTs	lo-lo-hi-lo
	417169	R13550	Hs.246773	ESTs	lo-lo-hi-lo
	443645	R36475	Hs.24321	Homo sapiens cDNA FLJ12028 fis, clone HE	lo-lo-hi-lo
	424878	H57111	Hs.221132	ESTs	lo-lo-hi-lo
30	449618	AI076459	Hs.15978	KIAA1272 protein	lo-lo-hi-lo
	432572	AI660840	Hs.191202	ESTs, Weakly similar to ALUE_HUMAN IIII	lo-lo-hi-lo
	400293	N51002	Hs.306480	Homo sapiens mRNA; cDNA DKFZp761E2112 (f	lo-lo-hi-lo
	431474	AL133990	Hs.190642	CEGP1 protein	lo-lo-hi-lo
	421674	T10707	Hs.296355	hypothetical protein FLJ23138	lo-lo-hi-lo
35	438494	AA908678	Hs.130183	ESTs	lo-lo-hi-lo
	425332	AA633306	Hs.127279	ESTs	lo-lo-hi-lo
	451411	AA017492	Hs.135655	EST	lo-lo-hi-lo
	419972	AL041465	Hs.182982	golgin-67	lo-lo-hi-lo
	434804	AA649530	Hs.348148	gb:ns44f05.s1 NCI_CGAP_Alv1 Homo sapiens	lo-lo-hi-lo
40	442832	AW206560	Hs.253569	ESTs	lo-lo-hi-lo
	408660	AA525775		ESTs, Moderately similar to PC4259 ferri	lo-lo-hi-lo
	432674	AA641092	Hs.257339	ESTs, Weakly similar to I38022 hypothe	lo-lo-hi-lo
	448150	AI472167		ESTs	lo-lo-hi-lo
	450468	AW379075	Hs.141742	Homo sapiens cDNA FLJ12211 fis, clone MA	lo-lo-hi-lo
45	452874	AK001061	Hs.30925	hypothetical protein FLJ10199	lo-lo-hi-lo
	412088	AI689496	Hs.108932	ESTs	lo-lo-hi-lo
	443451	AI057404	Hs.58698	ESTs	lo-lo-hi-lo
	453853	AL040600	Hs.188083	ESTs	lo-lo-hi-lo
	419863	AW952691	Hs.93485	Homo sapiens mRNA; cDNA DKFZp761D191 (fr	lo-lo-hi-lo
50	420729	AW964897	Hs.290825	ESTs	lo-lo-hi-lo
	440801	AA906366	Hs.190535	ESTs	lo-lo-hi-lo
	407284	AI539227	Hs.214039	hypothetical protein FLJ23556	lo-lo-hi-lo
	428279	AA425310	Hs.155766	ESTs, Weakly similar to A47582 B-cell gr	lo-lo-hi-lo
	436862	AI821940		ESTs, Moderately similar to ALU8_HUMAN A	lo-lo-hi-lo
55	432340	AA534222		gb:ncj21c02.s1 NCI_CGAP_AA1 Homo sapiens	lo-lo-hi-lo
	442048	AA974603		gb:op34f05.s1 Soares_NFL_T_GBC_S1 Homo s	lo-lo-hi-lo
	418781	T41160	Hs.8404	ESTs	lo-lo-hi-lo
	450642	R39773	Hs.7130	copine IV	lo-lo-hi-lo
	451661	AB020650	Hs.26777	Homo sapiens, Similar to KIAA0643 protei	lo-lo-hi-lo
60	435812	AA700439	Hs.188490	ESTs	lo-lo-hi-lo
	448065	AI459177	Hs.172759	ESTs, Moderately similar to ALU7_HUMAN A	lo-lo-hi-lo
	453486	AL039201	Hs.173554	ubiquinol-cytochrome c reductase core pr	lo-lo-hi-lo
	414312	AA155694	Hs.191060	ESTs	lo-lo-hi-lo
	438980	AW502384		gb:U1-HF-BRDp-aka-f-12-0-ULr1 NIH_MGC_5	lo-lo-hi-lo
65	408001	AA046458	Hs.95296	ESTs	lo-lo-hi-lo
	421476	AW953805	Hs.21887	ESTs	lo-lo-hi-lo
	414426	D60745	Hs.25925	Homo sapiens, clone MGC:15393, mRNA, com	lo-lo-hi-lo
	444563	N57057	Hs.284163	ANKHZN protein	lo-lo-hi-lo
	418771	AA807881	Hs.25329	ESTs	lo-lo-hi-lo
70	417843	W07361	Hs.22545	Homo sapiens cDNA FLJ12935 fis, clone NT	lo-lo-hi-lo
	415565	AA642449	Hs.48994	ESTs, Weakly similar to AF151800 1 CGI-4	lo-lo-hi-lo
	419229	AI827237	Hs.282884	ESTs	lo-lo-hi-lo
	419905	AW248229	Hs.93659	protein disulfide isomerase related prot	lo-lo-hi-lo
	452870	AW502761	Hs.30909	KIAA0430 gene product	lo-lo-hi-lo
75	449059	AK000566	Hs.98135	hypothetical protein FLJ20559	lo-lo-hi-lo
	416157	NM_003243	Hs.342874	transforming growth factor, beta recepto	lo-lo-hi-lo
	439305	AW393883	Hs.98968	hypothetical protein FLJ23058	lo-lo-hi-lo
	419235	AW470411	Hs.288433	neurotrophin	lo-lo-hi-lo
	416640	BE262478	Hs.79404	neuron-specific protein	lo-lo-hi-lo
80	434938	AW500718	Hs.8115	Homo sapiens, clone MGC:16169, mRNA, com	lo-lo-hi-lo
	408177	AI241733	Hs.43871	ESTs	lo-lo-hi-lo
	438459	T49300	Hs.35304	Homo sapiens cDNA FLJ13655 fis, clone PL	lo-lo-hi-lo
	418381	AA682393	Hs.119237	ESTs	lo-lo-hi-lo
	432161	AK000400	Hs.341181	ESTs, Weakly similar to envelope [H.sapi	lo-lo-hi-lo
	418283	S79895	Hs.83942	cathepsin K (pseudosynthesis)	lo-lo-hi-lo
	421443	BE550141	Hs.156148	hypothetical protein FLJ13231	lo-lo-hi-lo

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5	416619	AF013168	Hs.79393	tuberous sclerosis 1	lo-lo-hi-lo
	449802	AW901804	Hs.23984	hypothetical protein FLJ20147	lo-lo-hi-lo
	446714	W73818	Hs.110028	ESTs	lo-lo-hi-lo
	413195	AA127382	Hs.22404	protease, serine, 12 (neurolypsin, moto	lo-lo-hi-lo
	438233	W52448	Hs.56147	ESTs	lo-lo-hi-lo
	416051	AA835868	Hs.25253	mannosidase, alpha, class 1A, member 1	lo-lo-hi-lo
	438855	AW946276	Hs.6441	Homo sapiens mRNA; cDNA DKFZp596J021 (fr	lo-lo-hi-lo
	425907	AA365752	Hs.155965	ESTs	lo-lo-hi-lo
10	451295	AI557212	Hs.17132	ESTs, Moderately similar to i54374 gene	lo-lo-hi-lo
	415443	T07353	Hs.7948	ESTs	lo-lo-hi-lo
	422366	T83882	Hs.97927	ESTs	lo-lo-hi-lo
	435163	AA668884	Hs.19155	ESTs	lo-lo-hi-lo
	426559	AB001914	Hs.170414	paired basic amino acid cleaving system	lo-lo-hi-lo
	448988	Y09763	Hs.22785	gamma-aminobutyric acid (GABA) A recepto	lo-lo-hi-lo
15	453655	AW960427	Hs.342874	transforming growth factor, beta recepto	lo-lo-hi-lo
	414516	AI307802	Hs.135560	ESTs, Weakly similar to T43458 hypotheti	lo-lo-hi-lo
	420028	AB014680	Hs.8786	carbohydrate (N-acetylglucosamine-6-O) s	lo-lo-hi-lo
	430223	NM_002514	Hs.235935	nephroblastoma overexpressed gene	lo-lo-hi-lo
20	425887	AL049443	Hs.161283	Homo sapiens mRNA; cDNA DKFZp596N2020 (f	lo-lo-hi-lo
	442577	AA292998	Hs.163900	ESTs	lo-lo-hi-lo
	424940	AA985308	Hs.283902	ESTs	lo-lo-hi-lo
	428839	AI767756	Hs.82302	Homo sapiens cDNA FLJ14614 fis, clone NT	lo-lo-hi-lo
	443868	W88483	Hs.293650	Homo sapiens mRNA for RGPR-p117, complet	lo-lo-hi-lo
	430334	AI824719	Hs.328700	ESTs	lo-lo-hi-lo
25	439686	W40445	Hs.235657	ESTs, Weakly similar to I38022 hypotheti	lo-lo-hi-lo
	423754	NM_016181	Hs.132526	melanoma antigen	lo-lo-hi-lo
	415205	H71616	Hs.135233	ESTs	lo-lo-hi-lo
	426413	AA377823		gb:EST90805 Synovial sarcoma Homo sapien	lo-lo-hi-lo
30	407204	R41933	Hs.140237	ESTs, Weakly similar to ALU1_HUMAN ALU S	lo-lo-hi-lo
	430234	N29317	Hs.236463	KIAA1238 protein	lo-lo-hi-lo
	437143	AW204056	Hs.8917	ESTs	lo-lo-hi-hi
	445162	AB011131	Hs.12376	piccolo (presynaptic cytomatrix protein)	lo-lo-hi-hi
	415083	AI632683	Hs.27179	Homo sapiens cDNA FLJ12933 fis, clone NT	lo-lo-hi-hi
35	442924	AA533513	Hs.93659	protein disulfide isomerase related prot	lo-lo-hi-hi
	429536	AA873016	Hs.206097	oncogene TC21	lo-lo-hi-hi
	458584	AF217518	Hs.324136	PTD012 protein	lo-lo-hi-hi
	419647	AA348947	Hs.91816	hypothetical protein	lo-lo-hi-hi
	427201	AB037860	Hs.173933	nuclear factor I/A	lo-lo-hi-hi
40	428030	AI915228	Hs.11493	Homo sapiens cDNA FLJ13536 fis, clone PL	lo-lo-hi-hi
	411779	AA292811	Hs.72050	non-metastatic cells 5, protein expresse	lo-lo-hi-hi
	442482	NM_014039	Hs.8360	PTD012 protein	lo-lo-hi-hi
	417458	NM_005555	Hs.82173	TGFB inducible early growth response	lo-lo-hi-hi
	438021	AV653790	Hs.324275	WW domain-containing protein 1	lo-lo-hi-hi
45	409799	D11928	Hs.76845	phosphoserine phosphatase-like	lo-lo-hi-hi
	440676	NM_004987	Hs.112378	UIM and senescent cell antigen-like doma	lo-lo-hi-hi
	421437	AW821252	Hs.104336	hypothetical protein	lo-lo-hi-hi
	456362	AW973003	Hs.179909	hypothetical protein FLJ22995	lo-lo-hi-hi
	407686	AW901268	Hs.128043	chromosome 21 open reading frame 51	lo-lo-hi-hi
50	431129	AL137751	Hs.263671	Homo sapiens mRNA; cDNA DKFZp434I0812 (f	lo-lo-hi-hi
	431874	AW610031	Hs.323914	translocase of inner mitochondrial membr	lo-lo-hi-hi
	448072	AI459306	Hs.24308	ESTs	lo-lo-hi-hi
	436860	H12751	Hs.5327	PRO1914 protein	lo-lo-hi-hi
	448770	AA326683	Hs.21992	likely ortholog of mouse variant polyade	lo-lo-hi-hi
55	428044	AA093322	Hs.301404	RNA binding motif protein 3	lo-lo-hi-hi
	451468	AW503398	Hs.293663	ESTs, Moderately similar to I38022 hypot	lo-lo-hi-hi
	440278	BE560870	Hs.9052	ESTs, Weakly similar to 2004399A chromos	lo-lo-hi-hi
	441102	AA973905		intermediate filament protein syncollin	lo-lo-hi-hi
	423942	AF209704	Hs.135723	glycolipid transfer protein	lo-lo-hi-hi
60	426254	U91985	Hs.105658	DNA fragmentation factor, 45 kD, alpha p	lo-lo-hi-hi
	409324	W76202	Hs.343812	lipic acid synthetase	lo-lo-hi-hi
	431707	R21326	Hs.267905	hypothetical protein FLJ10422	lo-lo-hi-hi
	423335	AB018337	Hs.127287	KIAA0794 protein	lo-lo-hi-hi
	429200	AA447871	Hs.194215	ESTs, Weakly similar to I38022 hypotheti	lo-lo-hi-hi
65	429698	AW117322	Hs.42365	ESTs	lo-lo-hi-hi
	409604	AW444448	Hs.49124	ESTs	lo-lo-hi-hi
	431797	BE169641	Hs.270134	hypothetical protein FLJ20280	lo-lo-hi-hi
	437576	BE514383		prothymosin, alpha (gene sequence 28)	lo-lo-hi-hi
	415992	C05837	Hs.145807	hypothetical protein FLJ13593	lo-lo-hi-hi
70	456537	W24704	Hs.54773	ESTs	lo-lo-hi-hi
	417665	AW852858	Hs.22862	ESTs	lo-lo-hi-hi
	422292	AI815733	Hs.114360	transforming growth factor beta-stimulat	lo-lo-hi-hi
	421501	M29971	Hs.1384	O-6-methylguanine-DNA methyltransferase	lo-lo-hi-hi
	457952	U25750		Human chromosome 17q21 mRNA clone 1046:1	lo-lo-hi-hi
75	414630	BE410857	Hs.16064	gb:601301177F1 NIH_MGC_21 Homo sapiens c	lo-lo-hi-hi
	421590	T31811	Hs.110480	DC12 protein	lo-lo-hi-hi
	404956			C1003210*gi 6912582 ref NP_036524.1 ps	lo-lo-hi-hi
	436829	AW297958	Hs.163109	ESTs	lo-lo-hi-hi
	402106	AK002178		hypothetical protein FLJ11316	lo-lo-hi-hi
80	404384			NM_020632*Homo sapiens ATPase, H(+)-tra	lo-lo-hi-hi
	445123	AI762911	Hs.145369	ESTs	lo-lo-hi-hi
	401757			Target Exon	lo-lo-hi-hi
	439502	AA836672	Hs.130694	ESTs	lo-lo-hi-hi

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	400111		Eos Control	lo-lo-hi-hi
	405446	AI015709	Homo sapiens mRNA; cDNA DKFZp586I2022 (f	lo-lo-hi-hi
	401563		C15001262:g 7304981 ref NP_038528.1 ca	lo-lo-hi-hi
	402786		C1000887*:g 12732453 ref XP_011474.1 C	lo-lo-hi-hi
5	426484	AA379658	Hs.272759 KIAA1457 protein	lo-lo-hi-hi
	414343	AL036166	Hs.323378 coated vesicle membrane protein	lo-lo-hi-hi
	421970	AF227156	Hs.110103 RNA polymerase I transcription factor RR	lo-lo-hi-hi
	422592	BE081857	Hs.94211 rod1 (required for cell differentiation,	lo-lo-hi-hi
10	413431	AW246428	Hs.75355 ubiquitin-conjugating enzyme E2N (homoio	lo-lo-hi-hi
	426746	J03626	Hs.2057 uridine monophosphate synthetase (orotat	lo-lo-hi-hi
	400237		NM_001087*:Homo sapiens angio-associated	lo-lo-hi-hi
	402532		Target Exon	lo-lo-hi-hi
	402396		Target Exon	lo-lo-hi-hi
15	459649	AW298364	Hs.289292 ESTs	lo-lo-hi-hi
	401512		NM_014080:Homo sapiens dual oxidase-like	lo-lo-hi-hi
	448622	AL046508	Hs.270607 ESTs, Weakly similar to STK2_HUMAN GERIN	lo-lo-hi-hi
	400501		ENSP00000251912*:KIAA1617 protein (Fragm	lo-lo-hi-hi
	452324	W81486	Hs.58648 ESTs	lo-lo-hi-hi
20	453146	AI338952	Hs.32194 ESTs	lo-lo-hi-hi
	430445	AW892432	Hs.65307 ESTs	lo-lo-hi-hi
	401750		NM_012448*:Homo sapiens signal transduce	lo-lo-hi-hi
	435236	T03890	Hs.157208 ESTs, Highly similar to ARX MOUSE HOME0B	lo-lo-hi-hi
	400375	NM_014115	Hs.286232 NM_014115*:Homo sapiens PRO0113 protein	lo-lo-hi-hi
25	412151	AA100529	Hs.286232 Homo sapiens cDNA: FLJ23190 fis, clone L	lo-lo-hi-hi
	410498	AA355749	gb:EST64459 Jurkat T-cells V1 Homo sapie	lo-lo-hi-hi
	405044		NM_014630*:Homo sapiens KIAA0211 gene pr	lo-lo-hi-hi
	413169	AW161061	Hs.62954 ESTs, Weakly similar to zinc finger prot	lo-lo-hi-hi
	402101		ENSP00000217725*:Laminin alpha-1 chain p	lo-lo-hi-hi
30	455019	AW850818	gb:IL3-CT0220-091199-026-A03 CT0220 Homo	lo-lo-hi-hi
	446826	AK000626	Hs.16230 hypothetical protein FLJ20619	lo-lo-hi-hi
	412180	AW898791	Hs.118837 gb:CM0-NN0075-130400-332-f06 NN0075 Homo	lo-lo-hi-hi
	407273	AJ132560	gb:Homo sapiens mRNA for immunoblobulin	lo-lo-hi-hi
	452895	BE389229	Hs.30954 phosphomevalonate kinase	lo-lo-hi-hi
35	416117	H19480	Hs.268787 ESTs	lo-lo-hi-hi
	430934	AI792302	Hs.248141 potassium inwardly-rectifying channel, s	lo-lo-hi-hi
	416309	R84694	Hs.79194 cAMP responsive element binding protein	lo-lo-hi-hi
	444578	T80795	Hs.193702 ESTs	lo-lo-hi-hi
	401966		C17000574:g 8923190 ref NP_060178.1 hy	lo-lo-hi-hi
40	444850	AW444882	Hs.148483 ESTs	lo-lo-hi-hi
	403885		Target Exon	lo-lo-hi-hi
	405435		Target Exon	lo-lo-hi-hi
	422694	C06003	Hs.23782 hypothetical protein FLJ12847	lo-lo-hi-hi
	422912	AW405973	Hs.11637 ESTs	lo-lo-hi-hi
45	412748	BE083158	Hs.10862 Homo sapiens cDNA: FLJ23313 fis, clone H	lo-lo-hi-hi
	403704		Target Exon	lo-lo-hi-hi
	440507	H06994	gb:yl81b07.r1 Soares infant brain 1N1B H	lo-lo-hi-hi
	405503		C7000609*:g 628012 pi A53933 myosin I	lo-lo-hi-hi
	456123	R00602	gb:ye74c04.r1 Soares fetal liver: spleen	lo-lo-hi-hi
50	454261	AF216077	Hs.48376 Homo sapiens clone HB-2 mRNA sequence	lo-lo-hi-hi
	458956	BE220675	gb:ht88f11.x1 NCLCGAP_Lu24 Homo sapiens	lo-lo-hi-hi
	418367	AA326035	Hs.59236 hypothetical protein DKFZp434L0718	lo-lo-hi-hi
	444553	AI167530	Hs.149380 ESTs	lo-lo-hi-hi
	405811		NM_024810:Homo sapiens hypothetical prot	lo-lo-hi-hi
55	429461	AI168219	Hs.99311 ESTs, Weakly similar to HSJ2_HUMAN DNAJ	lo-lo-hi-hi
	423378	BE313601	Hs.164866 hypothetical protein FLJ22558	lo-lo-hi-hi
	458516	BE010749	Hs.255097 ESTs	lo-lo-hi-hi
	404039		ENSP00000247650*:Hypothetical 177.6 kDa	lo-lo-hi-hi
	454148	AW732837	Hs.42390 nasopharyngeal carcinoma susceptibility	lo-lo-hi-hi
60	412678	AA115575	Hs.114914 ESTs	lo-lo-hi-hi
	449298	AI911333	Hs.171689 ESTs	lo-lo-hi-hi
	405525		NM_002439*:Homo sapiens mutS (E. coli) h	lo-lo-hi-hi
	424576	BE154142	Hs.96833 ESTs	lo-lo-hi-hi
	451601	N92100	Hs.97437 centrosomal protein 1	lo-lo-hi-hi
65	422395	AA310177	Hs.103931 DKFZP434B0335 protein	lo-lo-hi-hi
	434333	AA186733	Hs.292154 stromal cell protein	lo-lo-hi-hi
	413509	BE145419	gb:IL5-HT0198-291099-009-E01 HT0198 Homo	lo-lo-hi-hi
	419504	AI088585	Hs.118904 ESTs	lo-lo-hi-hi
	448586	AF285120	Hs.283734 CGI-204 protein	lo-lo-hi-hi
70	401209		C12000519:g 7710046 ref NP_057914.1 ki	lo-lo-hi-hi
	423554	M90516	Hs.1674 glutamine-fructose-6-phosphate transamin	lo-lo-hi-hi
	439803	AA001021	Hs.6685 thyroid hormone receptor interactor 8	lo-lo-hi-hi
	424593	AA343729	gb:EST49730 Gall bladder I Homo sapiens	lo-lo-hi-hi
	408122	AI432652	Hs.42824 hypothetical protein FLJ10718	lo-lo-hi-hi
75	409958	NM_001623	Hs.57697 hyaluronan synthase 1	lo-lo-hi-hi
	408214	AL120445	Hs.77823 hypothetical protein FLJ21343	lo-lo-hi-hi
	421911	AL041520	gb:DKFZp434G2317_s1 434 (synonym: htes3)	lo-lo-hi-hi
	407813	AL120247	Hs.40109 KIAA0872 protein	lo-lo-hi-hi
	425211	M18667	Hs.18667 progastricin (pepsinogen C)	lo-lo-hi-hi
80	442772	AW503680	Hs.5957 Homo sapiens clone 24416 mRNA sequence	lo-lo-hi-hi
	419733	AW362955	Hs.224961 Homo sapiens cDNA FLJ14415 fis, clone HE	lo-lo-hi-hi
	428260	AW290886	Hs.86999 ESTs, Weakly similar to S65657 alpha-1C-	lo-lo-hi-hi
	427083	NM_006363	Hs.173497 Sec23 (S. cerevisiae) homolog B	lo-lo-hi-hi

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5	418583	AA604379	Hs.86211	hypothetical protein	lo-lo-hi-hi
	407355	AA846203	Hs.193974	ESTs, Weakly similar to ALU1_HUMAN ALU S	lo-lo-hi-hi
	454003	AA058944	Hs.116602	Homo sapiens, clone IMAGE:4154008, mRNA,	lo-lo-hi-hi
	425322	U63630	Hs.155637	protein kinase, DNA-activated, catalytic	lo-lo-hi-hi
	402240			Target Exon	lo-lo-hi-hi
10	421867	AA481073	Hs.109045	hypothetical protein FLJ10498	lo-lo-hi-hi
	408603	R25283	Hs.326416	Homo sapiens mRNA; cDNA DKFZp564H1916 (f	lo-lo-hi-hi
	437389	AL359587	Hs.271586	hypothetical protein DKFZp762M115	lo-lo-hi-hi
	457148	AF091035	Hs.184627	KIAA0118 protein	lo-lo-hi-hi
	400277			Eos Control	lo-lo-hi-hi
15	400995			C11000295*:g 12737279 ref XP_012163.1	lo-lo-hi-hi
	400818			Target Exon	lo-lo-hi-hi
	402758			C1001689*:g 12722636 ref XP_010672.1 e	lo-lo-hi-hi
	403708			Target Exon	lo-lo-hi-hi
	405610			ENSP00000241065*:CDNA	lo-lo-hi-hi
20	414242	AA749230	Hs.26433	dolichyl-phosphate (UDP-N-acetylglucosam	lo-lo-hi-hi
	420757	X78592	Hs.99915	androgen receptor (dihydrotestosterone r	lo-lo-hi-hi
	400985			C11002190*:g 12737279 ref XP_012163.1	lo-lo-hi-hi
	401192			Target Exon	lo-lo-hi-hi
	404407			Target Exon	lo-lo-hi-hi
25	401405			Target Exon	lo-lo-hi-hi
	403055			C2002219*:g 12737280 ref XP_006682.2 k	lo-lo-hi-hi
	404661			C9000306*:g 12737280 ref XP_006682.2 k	lo-lo-hi-hi
	433627	AF078866	Hs.284296	Homo sapiens cDNA: FLJ122993 fis, clone K	lo-lo-hi-hi
	410204	AJ243425	Hs.326035	early growth response 1	lo-lo-hi-hi
30	432642	BE297635	Hs.3069	heat shock 70kD protein 9B (mortalin-2)	lo-lo-hi-hi
	400769			Target Exon	lo-lo-hi-hi
	433980	AA137152	Hs.286049	phosphoserine aminotransferase	lo-lo-hi-hi
	403725			Target Exon	lo-lo-hi-hi
	413587	AA156164	Hs.286241	protein kinase, cAMP-dependent, regulato	lo-lo-hi-hi
35	422614	AI908006	Hs.295362	Homo sapiens cDNA FLJ14459 fis, clone HE	lo-lo-hi-hi
	400275			NM_006513*:Homo sapiens seryl-tRNA synth	lo-lo-hi-hi
	402810			NM_004930*:Homo sapiens capping protein	lo-lo-hi-hi
	452049	BE268289	Hs.27693	peptidylprolyl isomerase (cyclophilin)-I	lo-lo-hi-hi
	445677	H96577	Hs.5838	ras homolog gene family, member E	lo-lo-hi-hi
40	428770	AK001667	Hs.193128	hypothetical protein FLJ10805	lo-lo-hi-hi
	428403	AI393048	Hs.326159	leucine rich repeat (in FLII) interactin	lo-lo-hi-hi
	434647	W74158	Hs.103189	lipopolysaccharide specific response-68	lo-lo-hi-hi
	402807			ENSP00000235229:SEMB.	lo-lo-hi-hi
	413992	W26276	Hs.136075	RNA, U2 small nuclear	lo-lo-hi-hi
45	407191	AA608751		gb:ae56h07.s1 Stratagene lung carcinoma	lo-lo-hi-hi
	403328			Target Exon	lo-lo-hi-hi
	411984	NM_005419	Hs.72988	signal transducer and activator of trans	lo-lo-hi-hi
	451017	BE391847	Hs.181173	hypothetical protein MGC10771	lo-lo-hi-hi
	404108			C7000911*:g 4235142 gb AAD14470.1 (ACO	lo-lo-hi-hi
50	407819	R42185	Hs.102720	ESTs	lo-lo-hi-hi
	435876	AW612586	Hs.160271	G protein-coupled receptor 48	lo-lo-hi-hi
	436716	AI433540		gb:ti69g05.x1 NCL_CGAP_Kid11 Homo sapien	lo-lo-hi-hi
	401419			Target Exon	lo-lo-hi-hi
	424363	AW512144	Hs.346947	ESTs, Weakly similar to A48809 carboxyle	lo-lo-hi-hi
55	408666	AW292096	Hs.255036	ESTs	lo-lo-hi-hi
	415516	F11411		gb:HSC2WF081 normalized infant brain cDN	lo-lo-hi-hi
	423144	AW851527	Hs.253677	ESTs, Weakly similar to I38022 hypotheti	lo-lo-hi-hi
	452560	BE077084	Hs.99969	ESTs	lo-lo-hi-hi
	439827	AA846538	Hs.187389	ESTs	lo-lo-hi-hi
60	419709	AA255592	Hs.347973	ESTs, Weakly similar to alternatively sp	lo-lo-hi-hi
	413672	BE156536		gb:QV0-HT0368-310100-091-h10 HT0368 Homo	lo-lo-hi-hi
	425291	AA354572		gb:EST62857 Jurkat T-cells V Homo sapien	lo-lo-hi-hi
	427403	AA402107	Hs.257146	ESTs, Moderately similar to I38022 hypot	lo-lo-hi-hi
	430911	AW937461	Hs.255377	ESTs	lo-lo-hi-hi
65	435293	AI040777	Hs.117170	ESTs	lo-lo-hi-hi
	448490	AI523897	Hs.271692	ESTs, Weakly similar to I38022 hypotheti	lo-lo-hi-hi
	449539	W80363	Hs.58446	ESTs	lo-lo-hi-hi
	458082	AW978811	Hs.314451	ESTs, Weakly similar to ALU1_HUMAN ALU S	lo-lo-hi-hi
	459407	N92114		gb:za22h11.r1 Soares fetal liver spleen	lo-lo-hi-hi
70	423231	AA323486	Hs.271273	Homo sapiens cDNA FLJ12335 fis, clone MA	lo-lo-hi-hi
	450628	AW382884	Hs.204715	ESTs	lo-lo-hi-hi
	411690	AA669253	Hs.136075	RNA, U2 small nuclear	lo-lo-hi-hi
	414739	U83867	Hs.77196	spectrin, alpha, non-erythrocytic 1 (alp	lo-lo-hi-hi
	444169	AV648170	Hs.58756	ESTs	lo-lo-hi-hi
75	420911	U77413	Hs.100293	O-linked N-acetylglucosamine (GlcNAc) tr	lo-lo-hi-hi
	422195	AB007903	Hs.113082	KIAA0443 gene product	lo-lo-hi-hi
	452704	AA027823	Hs.149424	Homo sapiens PNAS-130 mRNA, complete cds	lo-lo-hi-hi
	425074	AA495930		Homo sapiens cDNA: FLJ22165 fis, clone H	lo-lo-hi-hi
	426376	N46752	Hs.302985	ESTs	lo-lo-hi-hi
80	447754	AW073310	Hs.163533	Homo sapiens cDNA FLJ14142 fis, clone MA	lo-lo-hi-hi
	413686	AI469213	Hs.71404	ESTs	lo-lo-hi-hi
	449000	U69560	Hs.3826	kelch-like protein C3IP1	lo-lo-hi-hi
	430064	AK000091	Hs.231436	hypothetical protein FLJ20084	lo-lo-hi-hi
	412205	N33818	Hs.20274	ESTs, Weakly similar to unnamed protein	lo-lo-hi-hi
	423855	AI420582	Hs.136164	cutaneous T-cell lymphoma-associated tum	lo-lo-hi-hi
	455619	BE063853		gb:QV3-BT0296-011299-022-g09 BT0296 Homo	lo-lo-hi-hi

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	408722	AA487860	Hs.298102	ESTs	
	459710	A1701596	Hs.121592	ESTs	lo-lo-hi-hi
	417918	AA209205	Hs.163754	hypothetical protein FLJ12606	lo-lo-hi-hi
5	402964			NM_022095*:Homo sapiens hypothetical C2H	lo-lo-hi-hi
	424387	A1739312	Hs.284163	ANKHZN protein	lo-lo-hi-hi
	427220	AF069517	Hs.173993	RNA binding motif protein 6	lo-lo-hi-hi
	410451	BE065687		gb:RC3-BT0316-270400-016-f10 BT0316 Homo	lo-lo-hi-hi
	400713			NM_006165*:Homo sapiens nuclear factor r	lo-lo-hi-hi
10	407218	AA095473	Hs.28505	ubiquitin-conjugating enzyme E2H (homolo	lo-lo-hi-hi
	449312	N71673	Hs.223666	ESTs	lo-lo-hi-hi
	419612	AI498267	Hs.110613	KIAA0421 protein	lo-lo-hi-hi
	455272	BE148152		gb:RC4-HT0231-041199-012-b04 HT0231 Homo	lo-lo-hi-hi
	401839			NM_005177*:Homo sapiens ATPase, H+ trans	lo-lo-hi-hi
15	440422	AW452696	Hs.130760	myosin phosphatase, target subunit 2	lo-lo-hi-hi
	436819	AA731746	Hs.120232	ESTs	lo-lo-hi-hi
	413644	BE154910	Hs.278793	ESTs, Weakly similar to Z195_HUMAN ZINC	lo-lo-hi-hi
	413939	AL047051	Hs.199961	ESTs, Weakly similar to ALU7_HUMAN ALU S	lo-lo-hi-hi
	448198	BE622100	Hs.209406	ESTs, Weakly similar to I38600 zinc fing	lo-lo-hi-hi
20	450488	AA009999	Hs.59159	ESTs, Moderately similar to HPV16 E1 pro	lo-lo-hi-hi
	433507	AI817336	Hs.191791	ESTs	lo-lo-hi-hi
	438996	AW748336	Hs.110613	KIAA0421 protein	lo-lo-hi-hi
	442789	AW904361	Hs.131191	ESTs, Weakly similar to ALU7_HUMAN ALU S	lo-lo-hi-hi
	407251	U67611		transaldolase 1	lo-lo-hi-hi
25	409051	AA080912		gb:zm04d03.r1 Stratagene hNT neuron (937	lo-lo-hi-hi
	409123	AA063403		gb:zm04d12.s1 Stratagene corneal stroma	lo-lo-hi-hi
	416225	AA577730	Hs.186684	ESTs, Weakly similar to PC4259 ferritin	lo-lo-hi-hi
	433735	AA608955	Hs.109653	ESTs	lo-lo-hi-hi
	434404	AW445034	Hs.256578	ESTs	lo-lo-hi-hi
30	446667	BE161878	Hs.224805	ESTs	lo-lo-hi-hi
	447982	H22953	Hs.137551	ESTs	lo-lo-hi-hi
	438890	AA827756	Hs.135049	ESTs, Weakly similar to ALU7_HUMAN ALU S	lo-lo-hi-hi
	427882	AA640987	Hs.193767	ESTs	lo-lo-hi-hi
	459680	H96982	Hs.42321	ESTs	lo-lo-hi-hi
35	416632	H69480	Hs.141304	ESTs	lo-lo-hi-hi
	453876	AW021748	Hs.110406	ESTs, Weakly similar to I38022 hypotheti	lo-lo-hi-hi
	414528	AA148950	Hs.188836	ESTs	lo-lo-hi-hi
	419902	AA804409	Hs.118920	ESTs	lo-lo-hi-hi
	409542	AA503020	Hs.36563	hypothetical protein FLJ22418	lo-lo-hi-hi
40	433560	AI925195	Hs.130891	hypothetical protein MGC4400	lo-lo-hi-hi
	447499	AW262580	Hs.147674	protocadherin beta 16	lo-lo-hi-hi
	435023	AI692552		gb:wd73f12.x1 NCL CGAP_Lu24 Homo sapiens	lo-lo-hi-hi
	412156	H29487	Hs.17110	Homo sapiens mRNA; cDNA DKFZp434C2016 (f	lo-lo-hi-hi
	414505	R45389	Hs.23558	ESTs, Weakly similar to A48042 lysosomal	lo-lo-hi-hi
45	404277			NM_019111*:Homo sapiens major histocompa	lo-lo-hi-hi
	414662	AL036058	Hs.76807	major histocompatibility complex, class	lo-lo-hi-hi
	444430	AI611153	Hs.6093	Homo sapiens cDNA: FLJ22783 fis, clone K	lo-lo-hi-hi
	445612	N94126	Hs.12969	hypothetical protein	lo-lo-hi-hi
	403739			ENSP00000251563*:UDP-glucuronosyltransfe	lo-lo-hi-hi
50	403740			NM_001076*:Homo sapiens UDP glycosyltran	lo-lo-hi-hi
	411064	T16987	Hs.125472	ESTs, Moderately similar to KIAA0677 pro	lo-lo-hi-hi
	429143	AA333327	Hs.197335	plasma glutamate carboxypeptidase	lo-lo-hi-hi
	443060	D78874	Hs.8944	procollagen C-endopeptidase enhancer 2	lo-lo-hi-hi
55	422749	W01076	Hs.278573	CD59 antigen p18-20 (antigen identified	lo-lo-hi-hi
	429441	AJ224172	Hs.204096	lipophilin B (uteroglobin family member)	lo-lo-hi-hi
	414382	AW380339	Hs.8058	hematopoietic PBX-interacting protein	lo-lo-hi-hi
	441560	F13386	Hs.7888	Homo sapiens clone 23736 mRNA sequence	lo-lo-hi-hi
	446106	AA377165	Hs.44833	ESTs	lo-lo-hi-hi
	452239	AW379378	Hs.170121	protein tyrosine phosphatase, receptor t	lo-lo-hi-hi
60	446374	AW968304	Hs.56156	ESTs	lo-lo-hi-hi
	412795	BE241753	Hs.74592	special AT-rich sequence binding protein	lo-lo-hi-hi
	430325	AF004562	Hs.239356	syntaxin binding protein 1	lo-lo-hi-hi
	426392	AW968324	Hs.17384	ESTs	lo-lo-hi-hi
	447448	BE244285		F-box only protein 29	lo-lo-hi-hi
65	415743	AA167664	Hs.14333	ESTs, Weakly similar to Z195_HUMAN ZINC	lo-lo-hi-hi
	431607	AB033097	Hs.183669	KIAA1271 protein	lo-lo-hi-hi
	411979	X85134	Hs.72984	retinoblastoma-binding protein 5	lo-lo-hi-hi
	453620	BE396163	Hs.25005	ESTs, Weakly similar to ALU5_HUMAN ALU S	lo-lo-hi-hi
	431099	Y13367	Hs.249235	phosphoinositide-3-kinase, class 2, alph	lo-lo-hi-hi
70	421687	AL035306	Hs.106823	hypothetical protein MGC14797	lo-lo-hi-hi
	439565	AF086386	Hs.146599	ESTs	lo-lo-hi-hi
	442349	W40516	Hs.132355	Homo sapiens cDNA: FLJ22119 fis, clone H	lo-lo-hi-hi
	410096	AW245200	Hs.267400	hypothetical protein MGC5540	lo-lo-hi-hi
	429447	AW812452	Hs.83286	ESTs, Weakly similar to S14747 sphingomy	lo-lo-hi-hi
75	431802	AL133570	Hs.270571	Homo sapiens mRNA; cDNA DKFZp434L201 (fr	lo-lo-hi-hi
	441715	AI929453	Hs.342655	Homo sapiens cDNA FLJ13289 fis, clone OV	lo-lo-hi-hi
	458230	BE311851	Hs.6639	KIAA1624 protein	lo-lo-hi-hi
	429788	AF082283	Hs.193516	B-cell CLL/lymphoma 10	lo-lo-hi-hi
	450818	AI740573	Hs.142827	P311 protein	lo-lo-hi-hi
80	419576	AK002060	Hs.91251	hypothetical protein FLJ11198	lo-lo-hi-hi
	400401	AF159093		Homo sapiens endogenous retrovirus RAN1	lo-lo-hi-hi
	427004	AI921573	Hs.213107	ESTs	lo-lo-hi-hi
	401178	AA046772		RNA binding motif protein, X chromosome	lo-lo-hi-hi

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5	423749	U09848	Hs.132390	zinc finger protein 36 (KOX 18)
	428898	AB033070	Hs.194408	KIAA1244 protein
	458258	AW406546	Hs.127971	ESTs
	429521	BE048708	Hs.50949	ESTs
	402185			Target Exon
10	415961	H10983	Hs.155919	ESTs
	457265	AB023212	Hs.225967	KIAA0995 protein
	412419	AW948630		gb:QV0-FT0001-050500-226-g05 FT0001 Homo
	438397	AA806478	Hs.123206	ESTs
	440509	BE410132	Hs.134202	ESTs, Weekly similar to T17279 hypotheti
15	423895	AA332215		gb:EST36124 Embryo, 8 week 1 Homo sapien
	400251			NM_004651*:Homo sapiens ubiquitin specif
	445094	AW296163	Hs.147296	ESTs
	432323	AK0011409	Hs.274356	hypothetical protein FLJ10547
	444290	AA262496		gb:z520f1.r1 NCL_CGAP_GCB1 Homo sapiens
20	435803	Z44194	Hs.4994	transducer of ERBB2, 2
	436905	N31273	Hs.42380	ESTs
	401849			Target Exon
	402249			C1900553*:g 12741444 ref XP_008888.2
	406180	AB018249		small inducible cytokine subfamily A (Cy
25	448176	AI672546	Hs.170507	ESTs
	409259	AW608930	Hs.52184	hypothetical protein FLJ20618
	467335	AW969834	Hs.303303	ESTs
	452444	BE144022		gb:MRQ-HT0165-191199-004-f05 HT0165 Homo
	405429			Target Exon
30	430103	AA465259		gb:aa33b03.r1 NCL_CGAP_GCB1 Homo sapiens
	439944	AA856767	Hs.124623	ESTs
	411283	AW852754		gb:PM1-CT0247-180100-009-c05 CT0247 Homo
	453195	R10085	Hs.130370	ESTs
	452654	BE004783		gb:MR2-BN0114-270400-004-e11 BN0114 Homo
35	425684	AF000989	Hs.159201	thymosin, beta 4, Y chromosome
	429452	A1949495	Hs.133958	Homo sapiens cDNA FLJ13202 fis, clone NT
	431709	AF220185	Hs.267923	uncharacterized hypothalamus protein HT0
	411701	BE181659		gb:QV1-HT0638-070500-191-g07 HT0638 Homo
	430729	A572560	Hs.301283	KIAA0793 gene product
40	447476	BE293466	Hs.20680	ESTs, Weekly similar to I38022 hypotheti
	450436	AW293661	Hs.131887	ESTs
	405365			CX001212*:g 7861932 gb AAF70445.1 (AF2
	419555	AA244416		gb:nc07d11.s1 NCL_CGAP_Pr1 Homo sapiens
	446103	U90918	Hs.13804	hypothetical protein I4462023.2
45	400986			NM_024085*:Homo sapiens hypothetical pro
	421494	BE245833	Hs.169854	gb:TCBAP1E1908 Pedlatic pre-B cell acut
	400210			Eos Control
	400234			NM_005336:Homo sapiens high density lipo
	400235			NM_005336:Homo sapiens high density lipo
50	405387			NM_022170*:Homo sapiens Williams-Beuren
	433075	NM_002959		sortilin 1
	406302			C16000922:g 7499103 pir T20903 hypothe
	428181	AA423976		gb:zv62h06.s1 Soares_testis_NHT Homo sap
	456629	AW891965	Hs.279789	histone deacetylase 3
55	426940	AA393537	Hs.98347	ESTs, Weekly similar to JC5308 testis-sp
	433555	AA535902	Hs.146211	Homo sapiens HERC2P7 pseudogene, partial
	421431	AA650117	Hs.283107	ESTs
	448631	AI554923		gb:te53h12.x1 Soares_NFL_T_GBC_S1 Homo s
	433521	T60807	Hs.112482	Homo sapiens unknown mRNA sequence
60	407187	AA446971		gb:zw85f11.s1 Soares_total_fetus_Nb2HF8_
	450739	A1732707	Hs.116506	ESTs, Weekly similar to ALU7_HUMAN ALU S
	440004	BE397117	Hs.120824	hypothetical protein FLJ21845
	403947	NM_005032		plastin 3 (T isoform)
	405529	AW410458		chromosome 11 open reading frame2
65	402163			C19001075*:g 4557179 gb AAD23607.1 AC00
	404663			ENSP00000251884:KIAA1521 protein (Fragme
	400220			Eos Control
	401444			Target Exon
	456824	BE143703		gb:MR0-HT0164-191199-004-f03 HT0164 Homo
70	400206			Eos Control
	458659	AW749895	Hs.332520	Homo sapiens mRNA; cDNA DKFpZ434A1014 (f
	428666	AL080190	Hs.189242	Homo sapiens mRNA; cDNA DKFpZ434A202 (fr
	428442	AA428638	Hs.98606	ESTs
	440151	AA688167		gb:ak38e07.s1 Soares_testis_NHT Homo sap
75	431046	AW854382	Hs.249126	Homo sapiens clone 24894 mRNA sequence
	443914	AI091173	Hs.122362	ESTs, Weekly similar to p40 [H.sapiens]
	402469			Target Exon
	418155	R45481	Hs.23719	ESTs, Weekly similar to I38022 hypotheti
	446893	AI610818	Hs.7110	ESTs
80	442336	AW340958	Hs.7572	ESTs
	421290	NM_014368	Hs.103137	LIM homeobox protein 6
	450374	AA397540	Hs.60293	Homo sapiens clone 122482 unknown mRNA
	402347			Target Exon
	415184	AA380436	Hs.211973	homolog of Yeast RRP4 (ribosomal RNA pro
	415632	U07805	Hs.78524	TcD37 homolog
	423718	AL119520	Hs.180737	Homo sapiens clone 23664 and 23905 mRNA

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	449140	AW013840	Hs.202092	ESTs	lo-lo-hi-lo
	431241	AA496799	Hs.36958	ESTs	lo-lo-hi-lo
	416631	H69466		gb:yr8807.r1 Soares fetal liver spleen	lo-lo-hi-lo
5	424168	L29277	Hs.321677	signal transducer and activator of trans	lo-lo-hi-lo
	401600	BE247275		U5 snRNP-specific protein, 116 kD	lo-lo-hi-lo
	420588	AF000982	Hs.147916	DEAD/H (Asp-Glu-Ala-Asp/His) box polypep	lo-lo-hi-lo
	414111	BE047679	Hs.152982	hypothetical protein FLJ13117	lo-lo-hi-lo
	417138	AA193646	Hs.65771	Homo sapiens chromosome 19, BAC CIT-HSPC	lo-lo-hi-lo
10	424318	AA476515	Hs.172723	ESTs	lo-lo-hi-lo
	455653	BE154075		gb:PM0-HT0339-200400-010-E05 HT0339 Homo	lo-lo-hi-lo
	451493	H38656	Hs.32854	ESTs	lo-lo-hi-lo
	457015	AA688058	Hs.261544	ESTs	lo-lo-hi-lo
	403654			NM_003071:Homo sapiens SWI/SNF related,	lo-lo-hi-lo
15	435203	AW957127	Hs.294027	ESTs	lo-lo-hi-lo
	409322	BE091159	Hs.22687	ESTs, Moderately similar to unnamed prot	lo-lo-hi-lo
	437764	AA767795	Hs.166832	ESTs	lo-lo-hi-lo
	432542	AW083920	Hs.16098	claudin 2	lo-lo-hi-lo
	436125	AA765895	Hs.152895	ESTs	lo-lo-hi-lo
20	403217	AL134878		ribosomal protein, large P2	lo-lo-hi-lo
	434023	AI277883	Hs.146141	ESTs	lo-lo-hi-lo
	442419	AI749893	Hs.270532	ESTs, Weakly similar to I38022 hypothe	lo-lo-hi-lo
	443667	AI129066	Hs.135457	ESTs	lo-lo-hi-lo
	451445	AA017609	Hs.343449	gb:ze37e01.r1 Soares retina N2b4HR Homo	lo-lo-hi-lo
25	454775	BE160229		gb:QV1-HT0413-090200-062-a12 HT0413 Homo	lo-lo-hi-lo
	411053	AW815061		gb:CM0-ST0209-271099-082-d10 ST0209 Homo	lo-lo-hi-lo
	435312	AJ243396	Hs.4865	voltage-gated sodium channel beta-3 subu	lo-lo-hi-lo
	450875	AK000724	Hs.301553	karyopherin alpha 6 (Importin alpha 7)	lo-lo-hi-lo
	451180	H61899	Hs.171937	steroid dehydrogenase-like	lo-lo-hi-lo
30	427327	AW501456	Hs.288283	Homo sapiens cDNA: FLJ22355 fis, clone H	lo-lo-hi-lo
	444321	AW204210	Hs.122275	Homo sapiens mRNA; cDNA DKFZp564N1623 (f	lo-lo-hi-lo
	405109	N47812		CGI-35 protein	lo-lo-hi-lo
	450182	AI796400	Hs.240767	Human DNA sequence from clone RP1-12G14	lo-lo-hi-lo
	424990	AU076896	Hs.154095	zinc finger protein 143 (clone pHZ-1)	lo-lo-hi-lo
35	428997	AF065391	Hs.194718	zinc finger protein 265	lo-lo-hi-lo
	402602			NM_021186*:Homo sapiens zona pellucida g	lo-lo-hi-lo
	428772	AI524039	Hs.192524	ESTs	lo-lo-hi-lo
	423759	AI142358	Hs.184361	ESTs, Moderately similar to ALU7_HUMAN A	lo-lo-hi-lo
	434350	AL042940	Hs.93872	KIAA1662 protein	lo-lo-hi-lo
40	442274	AI733484	Hs.129182	ESTs	lo-lo-hi-lo
	442884	AI076570	Hs.134053	ESTs	lo-lo-hi-lo
	400481			Target Exon	lo-lo-hi-lo
	407283	T51008		gb:yb55e08.s1 Stratagene ovary (937217)	lo-lo-hi-lo
	408859	AW291672	Hs.258981	ESTs	lo-lo-hi-lo
45	455615	BE045344	Hs.274923	ESTs, Moderately similar to unnamed prot	lo-lo-hi-lo
	427315	AA179949	Hs.175563	Homo sapiens mRNA; cDNA DKFZp564N0763 (f	lo-lo-hi-lo
	449375	R07114	Hs.271224	ESTs	lo-lo-hi-lo
	419937	AB040959	Hs.93836	DKFZP434N014 protein	lo-lo-hi-lo
	422231	AA443512	Hs.101383	ESTs	lo-lo-hi-lo
50	437210	AA311443	Hs.293563	Homo sapiens mRNA; cDNA DKFZp586E2317 (f	lo-lo-hi-lo
	418056	AA524886		gb:nh34f02.s1 NCL_CGAP_P3 Homo sapiens	lo-lo-hi-lo
	446586	N58790	Hs.268820	ESTs	lo-lo-hi-lo
	407949	W21874	Hs.247057	ESTs, Weakly similar to 2109260A B cell	lo-lo-hi-lo
	440296	D30829	Hs.180610	splicing factor proline/glutamine rich (lo-lo-hi-lo
55	422260	AA315993	Hs.105484	regenerating gene type IV	lo-lo-hi-lo
	434685	AA542445	Hs.287457	Homo sapiens cDNA FLJ11949 fis, clone HE	lo-lo-hi-lo
	412657	AW976165		gb:EST388274 MAGE resequences, MAGN Homo	lo-lo-hi-lo
	405188			Target Exon	lo-lo-hi-lo
	416954	AI222358		gb:qh04c12.x1 Soares_NFL_T_GBC_S1 Homo s	lo-lo-hi-lo
60	423700	AA232375	Hs.58606	SNRPN upstream reading frame	lo-lo-hi-lo
	430288	BE394943	Hs.13804	hypothetical protein dJ462023.2	lo-lo-hi-lo
	435184	T67162	Hs.135127	ESTs, Weakly similar to unnamed protein	lo-lo-hi-lo
	431475	AI567669	Hs.40342	putative nuclear protein	lo-lo-hi-lo
	445239	AI217375	Hs.170023	ESTs, Weakly similar to CA36_HUMAN COLLA	lo-lo-hi-lo
65	436151	AK000801	Hs.324271	Homo sapiens cDNA FLJ20794 fis, clone CO	lo-lo-hi-lo
	448489	AI523875		gb:tg97d04.x1 NCL_CGAP_CLL1 Homo sapiens	lo-lo-hi-lo
	424470	BE244261	Hs.323502	Homo sapiens cDNA: FLJ23539 fis, clone L	lo-lo-hi-lo
	434733	AI334367	Hs.159337	ESTs	lo-lo-hi-lo
	409469	AW517236	Hs.335762	ESTs	lo-lo-hi-lo
70	414034	U89277	Hs.305985	early development regulator 1 (homolog o	lo-lo-hi-lo
	420382	AW959165	Hs.270034	Homo sapiens, Similar to nuclear localiz	lo-lo-hi-lo
	430433	AA478883	Hs.273766	ESTs	lo-lo-hi-lo
	435351	T80177	Hs.118094	similar to rat nuclear ubiquitous caseln	lo-lo-hi-lo
	403218	AL134878		ribosomal protein, large P2	lo-lo-hi-lo
75	420678	AW593288	Hs.3530	TLS-associated serine-arginine protein 2	lo-lo-hi-lo
	445808	AV655234		ESTs, Moderately similar to PC4259 ferri	lo-lo-hi-lo
	429933	AA765596	Hs.187691	ESTs	lo-lo-hi-lo
	419802	AA250950	Hs.154334	ESTs	lo-lo-hi-lo
	425155	W26522	Hs.75890	gb:32g2 Human retina cDNA randomly prime	lo-lo-hi-lo
80	417314	N68168		gb:za11c01.s1 Soares fetal liver spleen	lo-lo-hi-lo
	428290	AI932995	Hs.183475	Homo sapiens clone 25061 mRNA sequence	lo-lo-hi-lo
	422128	AW881145		gb:QV0-OT0033-010400-182-a07 OT0033 Homo	lo-lo-hi-lo
	432014	H66741	Hs.38540	ESTs, Weakly similar to ALU4_HUMAN ALU S	lo-lo-hi-lo

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5	407351	AW363165		gb:PM3-HT0344-151299-004-f07 HT0344 Homo	lo-lo-hi-lo
	443231	W87548	Hs.132932	ESTs	lo-lo-hi-lo
	444001	AI095087	Hs.152299	ESTs, Moderately similar to S65657 alpha	lo-lo-hi-lo
	435064	T70740	Hs.31433	ESTs	lo-lo-hi-lo
	435173	AW295645	Hs.255451	ESTs	lo-lo-hi-lo
10	411831	AW994394		gb:RC3-BN0036-060400-014-h12 BN0036 Homo	lo-lo-hi-lo
	446572	AV659151	Hs.282961	ESTs	lo-lo-hi-lo
	428114	AI821548	Hs.98363	ESTs, Weakly similar to I38022 hypotheti	lo-lo-hi-lo
	406207			Target Exon	lo-lo-hi-lo
	405011			Target Exon	lo-lo-hi-lo
15	409451	AF012625	Hs.54472	fragile X mental retardation 2	lo-lo-hi-lo
	411233	AW833793		gb:QV4-TT0008-130100-080-a06 TT0008 Homo	lo-lo-hi-lo
	455729	BE072092		gb:PM4-BT0532-160200-003-b11 BT0532 Homo	lo-lo-hi-lo
	439454	AA836120	Hs.258958	ESTs	lo-lo-hi-lo
	445124	AI806403	Hs.143942	ESTs	lo-lo-hi-lo
20	410324	AW292539	Hs.30177	ESTs	lo-lo-hi-lo
	445548	AI769392	Hs.200215	ESTs	lo-lo-hi-lo
	416999	AW195747	Hs.21122	hypothetical protein FLJ11830 similar to	lo-lo-hi-lo
	414553	AI813865	Hs.164478	hypothetical protein FLJ21939 similar to	lo-lo-hi-lo
	444647	H14718	Hs.11506	Human clone 23589 mRNA sequence	lo-lo-hi-lo
25	418271	NM_000919	Hs.83920	peptidylglycine alpha-amidating monooxycg	lo-lo-hi-lo
	407939	W05608	Hs.312679	ESTs, Weakly similar to A49019 dynein he	lo-lo-hi-lo
	432676	AI187366		gb:qf29c01.x1 Soares_testis_NHT Homo sep	lo-lo-hi-lo
	415156	X84908	Hs.78060	phosphorylase kinase, beta	lo-lo-hi-lo
	432679	AI146956	Hs.146723	ESTs, Weakly similar to A53950 transcrip-	lo-lo-hi-lo
30	412121	AB033061	Hs.73287	KIAA1235 protein	lo-lo-hi-lo
	418858	AW961605	Hs.21145	hypothetical protein RG083M05.2	lo-lo-hi-lo
	425204	NM_002436	Hs.1861	membrane protein, palmitoylated 1 (55kD)	lo-lo-hi-lo
	418348	AI537157	Hs.95322	hypothetical protein FLJ23560	lo-lo-hi-lo
	410765	AI694972	Hs.56180	nucleosome assembly protein 1-like 2	lo-lo-hi-lo
35	445594	AW058463	Hs.12940	zinc-fingers and homeoboxes 1	lo-lo-hi-lo
	416503	H98502	Hs.269853	ESTs	lo-lo-hi-lo
	426167	AF039023	Hs.167496	RAN binding protein 6	lo-lo-hi-lo
	451752	AB032997	Hs.26966	KIAA1171 protein	lo-lo-hi-lo
	447124	AW976438	Hs.17428	RBP1-like protein	lo-lo-hi-lo
40	419872	AI422951	Hs.146162	ESTs	lo-lo-hi-lo
	443161	AI038316		gb:ox48c06.x1 Soares_tetal_fetus_Nb2HF8_	lo-lo-hi-lo
	445391	T92576	Hs.191168	ESTs	lo-lo-hi-lo
	443801	AW206942	Hs.253594	intron of: trichorhinophalangeal syndro	lo-lo-hi-lo
	446706	AW807631	Hs.190468	Homo sapiens, Similar to nuclear localiz	lo-lo-hi-lo
45	428172	U09367	Hs.182828	zinc finger protein 136 (clone pHZ-20)	lo-lo-hi-lo
	421021	AA608018	Hs.109302	ESTs	lo-lo-hi-lo
	431749	AL049263	Hs.306292	Homo sapiens mRNA; cDNA DKFZp564F133 (fr	lo-lo-hi-lo
	423784	AK000039	Hs.132826	Homo sapiens cDNA FLJ14913 fis, clone PL	lo-lo-hi-lo
	419479	AI288348	Hs.23450	mitochondrial ribosomal protein S25	lo-lo-hi-lo
50	450900	H61005	Hs.37902	ESTs	lo-lo-hi-lo
	423395	AI382555	Hs.127950	bromodomain-containing 1	lo-lo-hi-lo
	426137	AL040683	Hs.167031	DKFZP566D133 protein	lo-lo-hi-lo
	442012	AI733277	Hs.128321	ESTs	lo-lo-hi-lo
	452271	AA025976	Hs.34569	ESTs	lo-lo-hi-lo
55	414882	D79994	Hs.77546	Homo sapiens cDNA: FLJ21983 fis, clone H	lo-lo-hi-lo
	432195	AJ243669	Hs.8127	KIAA0144 gene product	lo-lo-hi-lo
	430217	N47863	Hs.180460	ribosomal protein S24	lo-lo-hi-lo
	429567	R35606	Hs.326900	Human EST clone 53125 mariner transposon	lo-lo-hi-lo
	438810	AW897846	Hs.5421	hypothetical protein DKFZp761N09121	lo-lo-hi-lo
60	436795	BE515260	Hs.5320	hypothetical protein	lo-lo-hi-lo
	426352	N72324	Hs.55098	ESTs	lo-lo-hi-lo
	415308	F05251		gb:HSC04H101 normalized infant brain cDN	lo-lo-hi-lo
	420148	U34227	Hs.95361	myosin VIIA (Usher syndrome 1B (autosoma	lo-lo-hi-lo
	434442	AA737415	Hs.152826	ESTs	lo-lo-hi-lo
65	449429	AA054224	Hs.59847	ESTs	lo-lo-hi-lo
	410245	C17908	Hs.194125	ESTs	lo-lo-hi-lo
	421168	AF182277	Hs.330780	cytochrome P450, subfamily IIB (phenobar	lo-lo-hi-lo
	436237	R11528	Hs.271968	ESTs	lo-lo-hi-lo
	440668	AI989538	Hs.191074	ESTs	lo-lo-hi-lo
70	422068	AI807519	Hs.104520	Homo sapiens cDNA FLJ13694 fis, clone PL	lo-lo-hi-lo
	410216	BE061839		gb:RC1-BT0254-290100-015-a05 BT0254 Homo	lo-lo-hi-lo
	439437	AI207788	Hs.343628	sialyltransferase 4B (beta-galactosidase	lo-lo-hi-lo
	417061	AI675944	Hs.188891	Homo sapiens cDNA FLJ12033 fis, clone HE	lo-lo-hi-lo
	403046			NM_005656: Homo sapiens transmembrane pr	lo-lo-hi-lo
75	404528	AI912555		peptide YY, 2 (seminalplasmin)	lo-lo-hi-lo
	439734	AC005013	Hs.149	cAMP response element-binding protein CR	lo-lo-hi-lo
	452997	N64777	Hs.44556	ESTs	lo-lo-hi-lo
	403745			ENSP00000226812: KIAA1494 protein (Fragm	lo-lo-hi-lo
	411448	AA178955	Hs.271439	ESTs, Weakly similar to I38022 hypotheti	lo-lo-hi-lo
80	422460	AW445014	Hs.197746	ESTs	lo-lo-hi-lo
	404058			Target Exon	lo-lo-hi-lo
	436184	BE154067	Hs.136660	ESTs, Weakly similar to ZN91_HUMAN ZINC	lo-lo-hi-lo
	427702	N76569	Hs.14454	ESTs, Weakly similar to TFIIID subunit TA	lo-lo-hi-lo
	440695	AW088363	Hs.245240	ESTs	lo-lo-hi-lo
	424881	AL119690	Hs.153618	HCGV111-1 protein	lo-lo-hi-hi
	440573	BE550891	Hs.270624	ESTs	lo-lo-hi-hi

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	416659	W22048	Hs.84753	gb:61A12 Human retina cDNA Tsp509I-cleav	lo-lo-hi-hi
	436731	AA580691	Hs.180789	S164 protein	lo-lo-hi-hi
	405102			C15001220*.gij4469568[gj]AAD21311.1] (AF	lo-lo-hi-hi
5	450219	A1826999	Hs.224624	ESTs	lo-lo-hi-hi
	404527	A1912555		peptide YY, 2 (seminalplasmin)	lo-lo-hi-hi
	439158	R60323	Hs.193888	ESTs	lo-lo-hi-hi
	431952	Z70695	Hs.272240	Homo sapiens cDNA FLJ11086 fis, clone PL	lo-lo-hi-hi
	418584	NM_004606	Hs.1179	TATA box binding protein (TBP)-associate	lo-lo-hi-hi
10	424241	AW995948	Hs.182339	Homo sapiens pyruvate dehydrogenase kina	lo-lo-hi-hi
	410124	AW962229	Hs.128927	Homo sapiens cDNA FLJ13903 fis, clone TH	lo-lo-hi-hi
	435955	AA830515	Hs.222917	ESTs	lo-lo-hi-hi
	424001	W67883	Hs.137476	paternally expressed 10	hi-hi-lo-lo
	441399	A1630844	Hs.126919	ESTs	hi-hi-lo-lo
	440184	AB002297	Hs.7022	dedicator of cyto-kinesis 3	hi-hi-lo-lo
15	421996	AW583807	Hs.1460	glucagon	hi-hi-lo-lo
	444252	R21135	Hs.54985	ESTs	hi-hi-lo-lo
	402082			C18000743*.gij6678363[ref]NP_033416.1] t	hi-hi-lo-lo
	405396			C22000452*.gij6981522[ref]NP_036781.1] r	hi-hi-lo-lo
20	412457	T32587	Hs.170414	paired basic amino acid cleaving system	hi-hi-lo-lo
	415808	R21439	Hs.334578	Homo sapiens, clone IMAGE:3929520, mRNA	hi-hi-lo-lo
	441494	AW462344	Hs.129977	ESTs	hi-hi-lo-lo
	437330	AL353944	Hs.50115	Homo sapiens mRNA; cDNA DKFZp761J1112 (f	hi-hi-lo-lo
	452784	BE463857	Hs.151258	hypothetical protein FLJ21062	hi-hi-lo-lo
25	410037	AB020725	Hs.58009	KIAA0918 protein	hi-hi-lo-lo
	449145	A1632122	Hs.198408	ESTs	hi-hi-lo-lo
	452487	AW207659	Hs.6630	Homo sapiens cDNA FLJ13329 fis, clone OV	hi-hi-lo-lo
	431031	AA830335	Hs.105273	ESTs	hi-hi-lo-lo
	427209	H06509	Hs.92423	KIAA1566 protein	hi-hi-lo-lo
30	434280	BE005398		gb:CM1-BN0116-150400-189-h02 BN0116 Homo	hi-hi-lo-lo
	418235	AW994005	Hs.337534	ESTs	hi-hi-lo-lo
	429201	X03178	Hs.198246	group-specific component (vitamin D bind	hi-hi-lo-lo
	416653	AA768553	Hs.193145	metallothionein 1E (functional)	hi-hi-lo-lo
	422501	AA354690	Hs.144967	ESTs	hi-hi-lo-lo
35	425087	R62424	Hs.126059	ESTs	hi-hi-lo-lo
	426798	AA385062	Hs.130260	ESTs	hi-hi-lo-lo
	443798	R07848	Hs.188522	ESTs	hi-hi-lo-lo
	427254	AL121523	Hs.97774	ESTs	hi-hi-lo-lo
	431657	A1345227	Hs.105448	ESTs, Weakly similar to B34087 hypotheti	hi-hi-lo-lo
40	409963	AA133590	Hs.250857	calcium/calmodulin-dependent protein kin	hi-hi-lo-lo
	446006	NM_004403	Hs.13530	deafness, autosomal dominant 5	hi-hi-lo-lo
	418259	AA215404		ESTs	hi-hi-lo-lo
	410173	AA706017	Hs.119944	ESTs	hi-hi-lo-lo
	436023	T81819	Hs.302251	ESTs	hi-hi-lo-lo
45	448428	AF282874	Hs.21201	nectin 3; DKFZP566B0846 protein	hi-hi-lo-lo
	430665	BE360122	Hs.157367	ESTs, Weakly similar to I78885 serine/th	hi-hi-lo-lo
	432559	AW452948	Hs.257831	ESTs	hi-hi-lo-lo
	451572	AA018556	Hs.268691	ESTs, Moderately similar to ALU2_HUMAN A	hi-hi-lo-lo
	456032	AW957446	Hs.301711	ESTs	hi-hi-lo-lo
50	438209	AL120689	Hs.6111	aryl-hydrocarbon receptor nuclear transi	hi-hi-lo-lo
	438337	AK002058	Hs.6166	hypothetical protein FLJ11196	hi-hi-lo-lo
	431795	AK002068	Hs.270124	Homo sapiens cDNA FLJ11226 fis, clone PL	hi-hi-lo-lo
	421114	AW975051	Hs.293156	ESTs, Weakly similar to I78885 serine/th	hi-hi-lo-lo
	431843	AA516420		ESTs, Weakly similar to I38022 hypotheti	hi-hi-lo-lo
55	440948	AW188311	Hs.128619	ESTs	hi-hi-lo-lo
	430105	X70297	Hs.2540	cholinergic receptor, nicotinic, alpha p	hi-hi-lo-lo
	439046	AA947354		gb:cd88e11.s1 NCL_CGAP_Ov2 Homo sapiens	hi-hi-lo-lo
	451491	A1872094	Hs.286221	Homo sapiens cDNA FLJ13741 fis, clone PL	hi-hi-lo-lo
	452789	AW081625	Hs.242561	ESTs	hi-hi-lo-lo
60	419829	A1824228	Hs.115185	ESTs, Moderately similar to PCA259 ferri	hi-hi-lo-lo
	449567	A1990790	Hs.188614	ESTs	hi-hi-lo-lo
	407787	N21307	Hs.13477	ESTs, Weakly similar to 1207289A reverse	hi-hi-lo-lo
	409091	AW970336	Hs.269423	ESTs	hi-hi-lo-lo
	435354	AA678267	Hs.117115	ESTs	hi-hi-lo-lo
65	444809	BE207568	Hs.208219	oculospanin	hi-hi-lo-lo
	422170	A1791949	Hs.112432	anti-Mullerian hormone	hi-hi-lo-lo
	453582	AW854339	Hs.33476	hypothetical protein FLJ11937	hi-hi-lo-lo
	435905	AW997484	Hs.5003	KIAA0456 protein	hi-hi-lo-lo
	443884	N20617	Hs.194397	leptin receptor	hi-hi-lo-lo
70	430027	AB023197	Hs.227743	KIAA0980 protein	hi-hi-lo-lo
	432582	A1623817	Hs.168457	ESTs	hi-hi-lo-lo
	417993	AW963705	Hs.301183	molecule possessing ankyrin repeats indu	hi-hi-lo-lo
	444930	BE185536	Hs.301183	molecule possessing ankyrin repeats indu	hi-hi-lo-lo
	427794	AA709186	Hs.99070	ESTs	hi-hi-lo-lo
75	410913	AL050367	Hs.66762	Homo sapiens mRNA; cDNA DKFZp564A026 (fr	hi-hi-lo-lo
	431992	NM_002742	Hs.2891	protein kinase C, mu	hi-hi-lo-lo
	447846	AA324057	Hs.77955	Homo sapiens cDNA: FLJ123527 fis, clone L	hi-hi-lo-lo
	430439	AL133561		DKFZP434B061 protein	hi-hi-lo-lo
	432621	A1298501	Hs.12807	ESTs, Weakly similar to T46428 hypotheti	hi-hi-lo-lo
80	431427	AK000401	Hs.252748	Homo sapiens cDNA FLJ20394 fis, clone KA	hi-hi-lo-lo
	408872	A1476139	Hs.13291	ESTs	hi-hi-lo-lo
	453200	AA033832	Hs.212433	ESTs	hi-hi-lo-lo
	411529	AA430348	Hs.317596	Homo sapiens cDNA FLJ12927 fis, clone NT	hi-hi-lo-lo

5	414483	R25513	Hs.10683	ESTs	hi-hi-lo-lo
	451273	NM_014811	Hs.26163	KIAA0549 gene product	hi-hi-lo-lo
	437052	AA861697	Hs.120591	ESTs	hi-hi-lo-lo
	440049	R06699	Hs.19769	hypothetical protein MGC4174	hi-hi-lo-lo
	429483	AA974832	Hs.126708	ESTs	hi-hi-lo-lo
10	411296	BE207307	Hs.10114	growth suppressor 1	hi-hi-lo-lo
	425188	AK002052	Hs.155071	hypothetical protein FLJ11190	hi-hi-lo-lo
	436315	BE390513	Hs.27935	hypothetical protein MGC4837	hi-hi-lo-lo
	400297	AI127076	Hs.306201	hypothetical protein DKFZp564O1278	hi-hi-lo-lo
	431089	BE041395	Hs.85146	ESTs, Weakly similar to unknown protein	hi-hi-lo-lo
15	418824	AW751661	Hs.53542	choreoacanthocytosis gene; KIAA0986 prot	hi-hi-lo-lo
	449226	AB002365	Hs.23311	KIAA0367 protein	hi-hi-lo-lo
	450149	AW969781	Hs.132863	Zic family member 2 (odd-paired Drosophi	hi-hi-lo-lo
	418443	NM_005239	Hs.85146	v-ets avian erythroblastosis virus E26 o	hi-hi-lo-lo
	458692	BE549905	Hs.231754	ESTs	hi-hi-lo-lo
20	410102	AW248508	Hs.279727	ESTs; homologue of PEM-3 [Ciona savignyi	hi-hi-lo-lo
	451052	AL110125	Hs.25910	Homo sapiens mRNA; cDNA DKFZp554C1416 (f	hi-hi-lo-lo
	407633	NM_007069	Hs.37189	similar to rat HREV107	hi-hi-lo-lo
	418941	AA452970	Hs.239527	E1B-55kDa-associated protein 5	hi-hi-lo-lo
	407059	X95406		gb:H.sapiens cyclin E gene.	hi-hi-lo-lo
25	455956	BE162704		gb:PM1-HT0454-301299-001-d08 HT0454 Homo	hi-hi-lo-lo
	437763	AA469369	Hs.5831	tissue inhibitor of metalloproteinase 1	hi-hi-lo-lo
	451404	AA460775	Hs.5295	ESTs, Weakly similar to T17248 hypotheti	hi-hi-lo-lo
	428494	AA233439	Hs.184634	hypothetical protein FLJ20005	hi-hi-lo-lo
	414957	D61283	Hs.45206	ESTs	hi-hi-lo-lo
30	456415	AI734051	Hs.277102	ESTs, Weakly similar to ALU1_HUMAN ALU S	hi-hi-lo-lo
	400183			Eos Control	hi-hi-lo-lo
	400158			ENSP00000244302:cDNA FLJ11591 fis, clon	hi-hi-lo-lo
	403893			ENSP00000237068:Prolocaderin alpha 6 p	hi-hi-lo-lo
	423809	AI223833	Hs.154483	ESTs	hi-hi-lo-lo
35	400170			Eos Control	hi-hi-lo-lo
	403291			Target Exon	hi-hi-lo-lo
	422026	U80736	Hs.110826	trinucleotide repeat containing 9	hi-hi-lo-lo
	417130	AW276858	Hs.81256	S100 calcium-binding protein A4 (calcium	hi-hi-lo-lo
	432472	AA548781	Hs.136418	ESTs	hi-hi-lo-lo
40	405231			C2001066:gi10257425[ref]NP_033892.1] CD	hi-hi-lo-lo
	400141			Eos Control	hi-hi-lo-lo
	428971	BE278404	Hs.285813	hypothetical protein FLJ11807	hi-hi-lo-lo
	422390	AW450893	Hs.121830	ESTs, Weakly similar to T42682 hypotheti	hi-hi-lo-lo
	425538	BE270918	Hs.164026	Homo sapiens, clone IMAGE:3534875, mRNA,	hi-hi-lo-lo
45	456972	AI054347	Hs.2017	ribosomal protein L38	hi-hi-lo-lo
	456622	AF205849	Hs.107740	Kruppel-like factor 2 (lung)	hi-hi-lo-lo
	418515	AI568453	Hs.19487	ESTs, Weakly similar to CNH_HUMAN CORN1	hi-hi-lo-lo
	448439	BE613082	Hs.28229	ARG99 protein	hi-hi-lo-lo
	445418	AW139377	Hs.127179	cryptic gene	hi-hi-lo-lo
50	402559	Z23024		Rho GTPase activating protein 1	hi-hi-lo-lo
	402575	Z23024		Rho GTPase activating protein 1	hi-hi-lo-lo
	420811	AA807544		ESTs, Weakly similar to B34323 GTP-bindi	hi-hi-lo-lo
	446627	AI973016	Hs.15725	hypothetical protein SBB148	hi-hi-lo-lo
	400247			Eos Control	hi-hi-lo-lo
55	430289	AK001952	Hs.238039	hypothetical protein FLJ11090	hi-hi-lo-lo
	400133			Eos Control	hi-hi-lo-lo
	418816	T29621	Hs.88778	carbonyl reductase 1	hi-hi-lo-lo
	433579	BE264473	Hs.284297	hypothetical protein from EUROIMAGE 1967	hi-hi-lo-lo
	401952			Target Exon	hi-hi-lo-lo
60	410349	AW663021	Hs.323445	ESTs, Weakly similar to T2D3_HUMAN TRANS	hi-hi-lo-lo
	417558	AF045229	Hs.82280	regulator of G-protein signalling 10	hi-hi-lo-lo
	446851	AW007332	Hs.10450	Homo sapiens cDNA: FLJ22063 fis, clone H	hi-hi-lo-lo
	404489			Target Exon	hi-hi-lo-lo
	405802			Target Exon	hi-hi-lo-lo
65	456266	L29073	Hs.198726	cold shock domain protein A	hi-hi-lo-lo
	457133	M54968		v-Ki-ras2 Kirsten rat sarcoma 2 viral on	hi-hi-lo-lo
	459330	C16931		gb:C16931 Clontech human aorta polyA mRN	hi-hi-lo-lo
	433041	BE265848	Hs.289080	colon cancer-associated protein Mic1	lo-lo-lo-hi
	446545	AI431798	Hs.164192	ESTs, Weakly similar to Y161_HUMAN HYPOT	lo-lo-lo-hi
70	414911	NM_000107	Hs.77602	damage-specific DNA binding protein 2 (4	lo-lo-lo-hi
	414682	AL021154	Hs.76884	inhibitor of DNA binding 3, dominant neg	lo-lo-lo-hi
	422311	AF073515	Hs.114948	cytokine receptor-like factor 1	lo-lo-lo-hi
	447329	BE090517		ESTs, Moderately similar to ALUR_HUMAN A	lo-lo-lo-hi
	412942	AL120344	Hs.75074	mitogen-activated protein kinase-activat	lo-lo-lo-hi
75	420747	BE294407	Hs.99910	phosphofructokinase, platelet	lo-lo-lo-hi
	431912	AI660552	Hs.76549	ESTs, Weakly similar to A56154 Abl subst	lo-lo-lo-hi
	446506	AI123118	Hs.15159	chemokine-like factor, alternatively spl	lo-lo-lo-hi
	408633	AW963372	Hs.46677	PRO2000 protein	lo-lo-lo-hi
	433675	AW977653	Hs.75319	ribonucleotide reductase M2 polypeptide	hi-hi-lo-lo
80	424560	AA158727	Hs.150555	protein predicted by clone 23733	hi-hi-lo-lo
	425234	AW152225	Hs.165909	ESTs, Weakly similar to I38022 hypotheth	hi-hi-lo-lo
	439815	AA206079	Hs.6693	hypothetical protein FLJ20420	hi-hi-lo-lo
	410174	AA306007	Hs.59461	DKFZP434C245 protein	hi-hi-lo-lo
	410442	X73424	Hs.63788	propionyl Coenzyme A carboxylase, beta p	hi-hi-lo-lo
	429190	H18650	Hs.92502	ESTs	hi-hi-lo-lo
	423619	T48691	Hs.249159	adrenergic, alpha-2A-, receptor	hi-hi-lo-lo

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	433754	AW753676	Hs.39982	ESTs	hi-lo-lo-hi
	421998	R74441	Hs.117176	poly(A)-binding protein, nuclear 1	hi-lo-lo-hi
	451593	AF151879	Hs.26706	CGI-121 protein	hi-lo-lo-hi
5	452092	BE245374	Hs.27842	hypothetical protein FLJ11210	hi-lo-lo-hi
	447425	AI963747	Hs.18573	acylphosphatase 1, erythrocyte (common)	hi-lo-lo-hi
	421654	AW163267	Hs.106469	suppressor of var1 (S.cerevisiae) 3-like	hi-lo-lo-hi
	432502	NM_014841	Hs.277585	KIAA0170 gene product	hi-lo-lo-hi
	429597	NM_003816	Hs.2442	a disintegrin and metalloproteinase doma	hi-lo-lo-hi
10	434203	BE262677	Hs.283558	hypothetical protein PRO1855	hi-lo-lo-hi
	438461	AW075485	Hs.285049	phosphoserine aminotransferase	hi-lo-lo-hi
	409142	AL136877	Hs.50758	SMC4 (structural maintenance of chromoso	hi-lo-lo-hi
	439574	AI469788	Hs.165190	ESTs	hi-lo-lo-hi
	438182	AW342140	Hs.182545	ESTs, Weakly similar to ALU1_HUMAN ALU S	hi-lo-lo-hi
	449103	T24968	Hs.23038	HSPC071 protein	hi-lo-lo-hi
15	421059	AI654133	Hs.30212	thyroid receptor interacting protein 15	hi-lo-lo-hi
	446939	AL133353	Hs.16906	CGI-32 protein	hi-lo-lo-hi
	408576	NM_003542	Hs.46423	H4 histone family, member G	hi-lo-lo-hi
	410073	AW408163	Hs.58488	calenin (cadherin-associated protein), a	hi-lo-lo-hi
20	450912	AW939251	Hs.25547	v-fos FBJ murine osteosarcoma viral onco	hi-lo-lo-hi
	434701	AA460479	Hs.321707	KIAA0742 protein	hi-lo-lo-hi
	450455	AL117424	Hs.25035	chloride intracellular channel 4	hi-lo-lo-hi
	451144	AW958103	Hs.51712	pyruvate dehydrogenase kinase, isoenzyme	hi-lo-lo-hi
	427390	AI432163	Hs.268231	Homo sapiens cDNA: FLJ23111 fis, clone L	hi-lo-lo-hi
25	451831	NM_001674	Hs.460	activating transcription factor 3	hi-lo-lo-hi
	406776	T15206	Hs.237164	ESTs, Highly similar to LDH-H_HUMAN L-LAC	hi-lo-lo-hi
	428157	AI738719	Hs.198427	hexokinase 2	hi-lo-lo-hi
	408096	BE250162	Hs.83765	dihydrofolate reductase	hi-lo-lo-hi
	418203	X54942	Hs.83758	CDC28 protein kinase 2	hi-lo-lo-hi
30	449338	H73444	Hs.394	adenomedullin	hi-lo-lo-hi
	422082	AA016188	Hs.111244	hypothetical protein	hi-lo-lo-hi
	407907	AI752235	Hs.41270	procollagen-lysine, 2-oxoglutarate 5-dio	hi-lo-lo-hi
	416655	AW958613	Hs.79428	BCL2/adenovirus E1B 19kD-interacting pro	hi-lo-lo-hi
	419551	AW582256	Hs.91011	anterior gradient 2 (Xenopus laevis) hom	hi-lo-lo-hi
35	434094	AA305599	Hs.238205	hypothetical protein PRO2013	hi-lo-lo-hi
	443951	F13272	Hs.111334	ferritin, light polypeptide	hi-lo-lo-hi
	422975	AA347720	Hs.122659	KIAA0264 protein	hi-lo-lo-hi
	430314	AA369601	Hs.239138	pre-B-cell colony-enhancing factor	hi-lo-lo-hi
	412664	AA421404	Hs.345868	nucleolar protein p40; homolog of yeast	hi-lo-lo-hi
40	408089	H59799	Hs.42644	thioredoxin-like	hi-lo-lo-hi
	409690	W45393	Hs.55888	activating transcription factor 7	hi-lo-lo-hi
	442332	AI693251	Hs.8248	Target CAT	hi-lo-lo-hi
	408388	AF091086	Hs.44553	hypothetical protein	hi-lo-lo-hi
	441252	AW360901	Hs.183047	hypothetical protein MGC4399	hi-lo-lo-hi
45	433069	X76732	Hs.3164	nucleobindin 2	hi-lo-lo-hi
	443837	AI984625	Hs.9884	spindle pole body protein	hi-lo-lo-hi
	426108	AA622037	Hs.166468	programmed cell death 5	hi-lo-lo-hi
	441181	AA416925	Hs.121076	peptidylprolyl isomerase (cyclophilin)-I	hi-lo-lo-hi
	447397	BE247676	Hs.18442	E-1 enzyme	hi-lo-lo-hi
50	427505	AA361562	Hs.178761	26S proteasome-associated pad1 homolog	hi-lo-lo-hi
	430287	AW182459	Hs.125759	ESTs, Weakly similar to LEU5_HUMAN LEUKE	hi-lo-lo-hi
	415857	AA666115	Hs.127797	Homo sapiens cDNA FLJ11381 fis, clone HE	hi-lo-lo-hi
	423198	M81933	Hs.1634	cell division cycle 25A	hi-lo-lo-hi
	407687	AK002011	Hs.37558	hypothetical protein FLJ11149	hi-lo-lo-hi
55	431374	BE258532	Hs.251871	CTP synthase	hi-lo-lo-hi
	413273	U76679	Hs.75257	stem-loop (histone) binding protein	hi-lo-lo-hi
	442799	AI564739	Hs.68505	ESTs	hi-lo-lo-hi
	443881	R64512	Hs.237146	hypothetical protein FLJ12752	hi-lo-lo-hi
	416209	AA236776	Hs.79078	MAD2 (mitotic arrest deficient, yeast, h	hi-lo-lo-hi
60	421834	BE543205	Hs.288771	DKFZP586A0522 protein	hi-lo-lo-hi
	411263	BE297802	Hs.69360	kinesin-like 6 (mitotic centromere-assoc	hi-lo-lo-hi
	413924	AL119964	Hs.75616	seledin-1	hi-lo-lo-hi
	450698	AF151076	Hs.25199	hypothetical protein	hi-lo-lo-hi
	439453	BE264974	Hs.6556	thyroid hormone receptor interactor 13	hi-lo-lo-hi
65	429612	AF062649	Hs.252587	pituitary tumor-transforming 1	hi-lo-lo-hi
	443426	AF098158	Hs.9329	chromosome 20 open reading frame 1	hi-lo-lo-hi
	452353	C18825	Hs.29191	epithelial membrane protein 2	hi-lo-lo-hi
	419879	Z17805	Hs.93554	Homer, neuronal immediate early gene, 2	hi-lo-lo-hi
	422363	T55979	Hs.115474	replication factor C (activator 1) 3 (38	hi-lo-lo-hi
70	416065	BE267931	Hs.78996	proliferating cell nuclear antigen	hi-lo-lo-hi
	424308	AW975531	Hs.154443	minichromosome maintenance deficient (S.	hi-lo-lo-hi
	447519	U46258	Hs.339665	ESTs	hi-lo-lo-hi
	437679	NM_014214	Hs.5753	inositol (myo)-1(or 4)-monophosphatase 2	hi-lo-lo-hi
	446636	AC002563	Hs.15767	citron (rho-interacting, serine/threonin	hi-lo-lo-hi
75	422094	AF129535	Hs.272027	F-box only protein 5	hi-lo-lo-hi
	440334	BE276112	Hs.71165	zinc finger protein 259	hi-lo-lo-hi
	421921	H83363	Hs.6820	translocase of inner mitochondrial membr	hi-lo-lo-hi
	422938	NM_001809	Hs.1594	centromere protein A (17kD)	hi-lo-lo-hi
	427719	AI393122	Hs.134726	ESTs	hi-lo-lo-hi
80	422283	AW411307	Hs.114311	CDC45 (cell division cycle 45, S.cerevis	hi-lo-lo-hi
	424840	D79987	Hs.153479	extra spindle poles, S. cerevisiae, homo	hi-lo-lo-hi
	418216	AA662240	Hs.283099	AF15q14 protein	hi-lo-lo-hi
	412140	AA219691	Hs.73525	RAB6 interacting, kinesin-like (rabkines	hi-lo-lo-hi

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5	418322	AA284166	Hs.84113	cyclin-dependent kinase inhibitor 3 (CDK	hi-lo-lo-hi
	428479	Y00272	Hs.334562	cell division cycle 2, G1 to S and G2 to	hi-lo-lo-hi
	449722	BE280074	Hs.23960	cyclin E1	hi-lo-lo-hi
	417933	X02308	Hs.82962	thymidylate synthetase	hi-lo-lo-hi
	433001	AF217513	Hs.279905	clone HQ0310 PRO0310p1	hi-lo-lo-hi
	413943	AW294416	Hs.144687	Homo sapiens cDNA FLJ12981 fis, clone NT	hi-lo-lo-hi
	424905	NM_002497	Hs.153704	NIMA (never in mitosis gene a)-related k	hi-lo-lo-hi
	422765	AW409701	Hs.1578	baculoviral IAP repeat-containing 5 (sur	hi-lo-lo-hi
10	425397	J04088	Hs.156346	topoisomerase (DNA) II alpha (170kD)	hi-lo-lo-hi
	444371	BE540274	Hs.239	forkhead box M1	hi-lo-lo-hi
	422956	BE545072	Hs.122679	ECT2 protein (Epithelial cell transformi	hi-lo-lo-hi
	444783	AK001468	Hs.62180	anillin (Drosophila Scraps homolog), act	hi-lo-lo-hi
	453884	AA355925	Hs.36232	KIAA0185 gene product	hi-lo-lo-hi
15	416980	AA381133	Hs.80684	high-mobility group (nonhistone chromoso	hi-lo-lo-hi
	442432	BE093589	Hs.38178	hypothetical protein FLJ23468	hi-lo-lo-hi
	417308	H60720	Hs.81892	KIAA0101 gene product	hi-lo-lo-hi
	433133	AB027249	Hs.104741	PDZ-binding kinase; T-cell originated pr	hi-lo-lo-hi
	432626	AA471098	Hs.278544	acetyl-Coenzyme A acetyltransferase 2 (a	hi-lo-lo-hi
20	441020	W79283	Hs.35962	ESTs	hi-lo-lo-hi
	412281	AI810054	Hs.14119	ESTs	hi-lo-lo-hi
	435602	AF217515	Hs.283532	uncharacterized bone marrow protein BM03	hi-lo-lo-hi
	400882			Target Exon	hi-lo-lo-hi
	446269	AW263155	Hs.14559	hypothetical protein FLJ10540	hi-lo-lo-hi
25	417847	AI521558	Hs.7331	hypothetical protein FLJ22316	hi-lo-lo-hi
	400881			NM_025080:Homo sapiens hypothetical prot	hi-lo-lo-hi
	419356	AI656166	Hs.7331	hypothetical protein FLJ22316	hi-lo-lo-hi
	400292	AA250737	Hs.72472	BMP-R1B	hi-lo-lo-hi
	415539	AI733881	Hs.72472	BMP-R1B	hi-lo-lo-hi
30	453935	AI633770	Hs.42572	ESTs	hi-lo-lo-hi
	420005	AW271106	Hs.133294	ESTs	hi-lo-lo-hi
	428450	NM_014791	Hs.184339	KIAA0175 gene product	hi-lo-lo-hi
	436291	BE568452	Hs.344037	protein regulator of cytokinesis 1	hi-lo-lo-hi
	441352	BE614410	Hs.23044	RAD51 (S. cerevisiae) homolog (E coli Re	hi-lo-lo-hi
35	428484	AF104032	Hs.184601	solute carrier family 7 (cationic amino	hi-lo-lo-hi
	418526	BE019020	Hs.85838	solute carrier family 16 (monocarboxylic	hi-lo-lo-hi
	458809	AW972512	Hs.20985	sln3-associated polypeptide, 30kD	hi-lo-lo-hi
	444984	HI5474	Hs.132898	fatty acid desaturase 1	hi-lo-lo-hi
	447342	AI199268	Hs.19322	Homo sapiens, Similar to RIKEN cDNA 2010	hi-hi-lo-lo
40	428330	L22524	Hs.2256	matrix metalloproteinase 7 (matrilysin,	hi-hi-lo-lo
	428336	AA503115	Hs.183752	microseminoprotein, beta-	hi-hi-lo-lo
	430389	AL117429	Hs.240845	DKFZP434D146 protein	hi-hi-lo-lo
	417318	AW953937	Hs.240845	ESTs	hi-hi-lo-lo
	422545	X02761	Hs.287820	fibronectin 1	hi-hi-lo-lo
	417640	D30857	Hs.82353	protein C receptor, endothelial (EPCR)	hi-lo-lo-lo
45	422809	AK001379	Hs.121028	hypothetical protein FLJ10549	hi-lo-lo-lo
	425580	L11144	Hs.1907	galanin	hi-lo-lo-hi
	416836	D54745	Hs.80247	cholecystokinin	hi-lo-lo-hi
	434170	AA626509	Hs.122329	ESTs	hi-lo-lo-hi
50	427958	AA416000	Hs.98280	potassium intermediate/small conductance	hi-lo-lo-hi
	439706	AW872527	Hs.59751	ESTs, Weakly similar to DAF1_HUMAN DEATH	hi-lo-lo-hi
	450088	AW292933	Hs.254110	ESTs	hi-lo-lo-hi
	414219	W20010	Hs.75923	ALL1-fused gene from chromosome 1q	hi-lo-lo-hi
	419201	M22324	Hs.1239	alanyl (membrane) aminopeptidase (aminop	hi-lo-lo-hi
55	426263	AI908774	Hs.259785	camitine palmitoyltransferase I, liver	hi-lo-lo-hi
	456236	AF045229	Hs.82280	regulator of G-protein signalling 10	hi-lo-lo-hi
	456607	AI660190	Hs.105070	cyclin-dependent kinase inhibitor 1C (p5	hi-lo-lo-hi
	408437	AW957744	Hs.278469	lacrimal prolaine rich protein	hi-lo-lo-hi
	421180	BE410992	Hs.258730	heme-regulated initiation factor 2-alpha	hi-lo-lo-hi
60	413437	BE313164	Hs.75361	gene from NF2/meningioma region of 22q12	hi-lo-lo-hi
	432415	T16971	Hs.289014	ESTs, Weakly similar to A43932 mucin 2 p	hi-lo-lo-hi
	449230	BE613348	Hs.211579	melanoma cell adhesion molecule	hi-lo-lo-hi
	417979	AU077284	Hs.83081	GTP cyclohydrolase I feedback regulatory	hi-lo-lo-hi
	421877	AW250380	Hs.109059	mitochondrial ribosomal protein L12	hi-lo-lo-hi
65	412482	AI499930	Hs.334885	mitochondrial GTP binding protein	hi-lo-lo-hi
	428423	AU076517	Hs.184276	solute carrier family 9 (sodium/hydrogen	hi-lo-lo-hi
	422947	AA306782	Hs.122552	G-2 and S-phase expressed 1	hi-lo-lo-hi
	441072	AW275430	Hs.39504	hypothetical protein MGC4308	hi-lo-lo-hi
	415938	BE383507	Hs.78921	A kinase (PRKA) anchor protein 1	hi-lo-lo-hi
70	432278	AL137506	Hs.274256	hypothetical protein FLJ23563	hi-lo-lo-hi
	446651	AA393907	Hs.97179	ESTs	hi-lo-lo-hi
	431515	NM_012152	Hs.258583	endothelial differentiation, lysophospha	hi-lo-lo-hi
	445345	AW003850	Hs.12532	chromosome 1 open reading frame 21	hi-lo-lo-hi
	458965	AA010319	Hs.60389	ESTs	hi-lo-lo-hi
75	438321	AA576635	Hs.6153	CGL-48 protein	hi-lo-lo-hi
	416783	AA206186	Hs.79889	monocyte to macrophage differentiation-a	hi-lo-lo-hi
	453563	AW608906	Hs.181163	hypothetical protein MGC5629	hi-lo-lo-hi
	432393	AW205863	Hs.133988	hypothetical protein FKSG28	hi-lo-lo-hi
	433914	AF108138	Hs.112160	Homo sapiens DNA helicase homolog (PIF1)	hi-lo-lo-hi
80	414907	X90725	Hs.77597	polo (Drosophila)-like kinase	hi-lo-lo-hi
	432375	BE536069	Hs.2962	S100 calcium-binding protein P	hi-lo-lo-hi
	440773	AA352702	Hs.37747	Homo sapiens, Similar to RIKEN cDNA 2700	hi-lo-lo-hi
	415994	NM_002923	Hs.78944	regulator of G-protein signalling 2, 24k	hi-lo-lo-hi

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	412722	AI343300	Hs.15091	ESTs	hi-lo-lo-hi
	446839	BE091926	Hs.16244	mitotic spindle coiled-coil related prot	hi-lo-lo-hi
	428862	NM_000346	Hs.2316	SRY (sex determining region Y)-box 9 (ca	hi-lo-lo-hi
5	439108	AW163034	Hs.6467	synaplogrin 3	hi-lo-lo-hi
	430178	AW449612	Hs.152475	ESTs	hi-lo-lo-hi
	421733	AL119671	Hs.1420	fibroblast growth factor receptor 3 (ach	hi-lo-lo-hi
	452410	AL133619		Homo sapiens mRNA; cDNA DKFZp434E2321 (f	hi-lo-lo-hi
	430132	AA204686	Hs.234149	hypothetical protein FLJ20647	hi-lo-lo-hi
10	428297	AA236291	Hs.183583	serine (or cysteine) proteinase inhibitor	hi-lo-lo-hi
	413142	M81740	Hs.75212	ornithine decarboxylase 1	hi-lo-lo-hi
	427239	BE270447	Hs.174070	ubiquitin carrier protein	hi-lo-lo-hi
	409738	BE222975	Hs.56205	Insulin Induced gene 1	hi-lo-lo-hi
	410748	BE363816	Hs.12532	chromosome 1 open reading frame 21	hi-lo-lo-hi
	424506	AF220490	Hs.149623	group III secreted phospholipase A2	hi-lo-lo-hi
15	447333	BE090580	Hs.70704	hypothetical protein dJ616B8.3	hi-lo-lo-hi
	414761	AU077228	Hs.77256	enhancer of zeste (Drosophila) homolog 2	hi-lo-lo-hi
	419602	AW248434	Hs.91521	hypothetical protein	hi-lo-lo-hi
	411669	BE612676	Hs.303116	stromal cell-derived factor 2-like 1	hi-lo-lo-hi
	452322	BE566343	Hs.28988	glutaredoxin (thioltransferase)	hi-lo-lo-hi
20	426006	R49031	Hs.22627	ESTs	hi-lo-lo-hi
	457465	AW301344	Hs.122908	DNA replication factor	hi-lo-lo-hi
	406867	AA157857	Hs.182265	keratin 19	hi-lo-lo-hi
	407230	AA157857	Hs.182265	keratin 19	hi-lo-lo-hi
	446631	AJ003624	Hs.15896	kendrin	hi-lo-lo-hi
25	408493	BE206854	Hs.46039	phosphoglycerate mutase 2 (muscle)	hi-lo-lo-hi
	439186	AI697274	Hs.105435	GDP-mannose 4,6-dehydratase	hi-lo-lo-hi
	424544	M88700	Hs.150403	dopa decarboxylase (aromatic L-amino acid	hi-lo-lo-hi
	431325	AW026751	Hs.5794	ESTs, Weakly similar to 2109260A B cell	hi-lo-lo-hi
	414922	D00723	Hs.77631	glycine cleavage system protein H (amino	hi-lo-lo-hi
30	438291	BE514605	Hs.289092	Homo sapiens cDNA: FLJ22380 fis, clone H	hi-lo-lo-hi
	418574	N28754		M-phase phosphoprotein 9	hi-lo-lo-hi
	409342	AU077058	Hs.54089	BRCA1 associated RING domain 1	hi-lo-lo-hi
	432734	AA637396	Hs.263925	US1-interacting protein NUDE1, rat homo	hi-lo-lo-hi
	436087	BE300296	Hs.5054	CGL-133 protein	hi-lo-lo-hi
35	420309	AW043637	Hs.21766	ESTs, Weakly similar to ALU5_HUMAN ALU S	hi-lo-lo-hi
	411619	AI418609	Hs.71040	hypothetical protein FLJ20425	hi-lo-lo-hi
	424381	AA285249	Hs.146329	protein kinase Chk2	hi-lo-lo-hi
	442547	AA306997	Hs.217484	ESTs, Weakly similar to ALU1_HUMAN ALU S	hi-lo-lo-hi
	430376	AW292053	Hs.12532	chromosome 1 open reading frame 21	hi-lo-lo-hi
40	434666	AF151103	Hs.112259	T cell receptor gamma locus	hi-lo-lo-hi
	412330	NM_005100	Hs.788	A kinase (PRKA) anchor protein (gravin)	hi-lo-lo-hi
	452123	AI267615	Hs.38022	ESTs	hi-lo-lo-hi
	424893	AW295112	Hs.153648	Homo sapiens cDNA FLJ13303 fis, clone OV	hi-lo-lo-hi
	428057	AI343641	Hs.185798	ESTs	hi-lo-lo-hi
45	431566	AF176012	Hs.260720	J domain containing protein 1	hi-lo-lo-hi
	439979	AW600291	Hs.6823	hypothetical protein FLJ10430	hi-lo-lo-hi
	418836	AI655499	Hs.161712	ESTs	hi-lo-lo-hi
	433757	AI949974	Hs.152670	ESTs	hi-lo-lo-hi
	425236	AW067800	Hs.155223	stanniocalcin 2	hi-lo-lo-hi
50	426215	AW963419	Hs.155223	stanniocalcin 2	hi-lo-lo-hi

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TABLE 2B

Pkey: Unique Eos probeset identifier number
CAT number: Gene cluster number
Accession: Genbank accession numbers

5	Pkey	CAT Number	Accession
	408660	107294_1	AA525775 AA056342 AI538978 AW975281 AA664986
	409051	109699_1	AA080912 AA075318 AA063403 AA076594 AA078992 AA084926 AA081881 AA113913 AA113892 AA083821 AA134801 AA082953 AA070343
10			AA062835 AA075419 AA063293 AA071252 AA078900 AA062836 AW974305
	409123	110143_1	AA063403 AA070823 AA070060
	410216	1184664_1	BE061839 AW858663 AW606085
	410451	1204118_1	BE065667 BE065637 AW749002 H73690
	410498	120611_1	AA355749 AA085520 AW966333 AA340319 BE170936
15			AW815061 H71965 AW815072 AW815048 AW815041 AW815047 BE152831 BE152490 BE149043 BE149075 BE149035 BE149067
	411053	1230446_1	AW833793 AW833799 AW833346 AW833371 AW833795 AW833562 AW833667 AW833377
	411233	1236369_1	AW852754 AW852897 AW852757 AW852617 BE172755 AW835444
	411283	1237666_1	BE181659 AW890576 AW857638
	411701	1254466_1	AW994394 AW865900 AW865905 AW865891 AW866014 AW865898
20			AW948630 AW948626 AW948634 AW948616 AW948627 AW948615 AW948631 AW948605 AW948611 AW948610 AW948633 AW948623
	411831	1260400_1	AW948628 AW948604 AW948602 AW948607
	412419	1293418_1	AW962604 AA368639 AA112257
	412492	130082_1	AW976165 C04000
	412657	1318507_1	BE086815 BE086823 R81218 R69229
25			BE145419 BE145433
	413351	1363660_1	BE156536 BE156439 BE156700 BE156449 BE156653 BE156533 BE156524 BE156670 BE156721 BE156723
	413509	1374313_1	F05251 R13748 Z44028 H14747
	413672	1382512_1	F11411 R15237 Z43915 H20760
	415308	1533673_1	R39769 T53143 H60012
30			H69466 H93884 N59684
	415516	1539185_1	AI222358 N73390 D61648 AA243520 AA190953
	416508	1597894_1	N68168 N69188 N90450
	416631	1605019_1	AA524886 AW971347 AA211537
	416954	163427_1	AA215404 AI990909 BE464132 AW271459 N74332 AI262061
	417314	1666649_1	N28754 N28747 AI568146 AI979339 AA322671 AA322672 AW955043 AI990326 AA776406 AI016250 AA843678 AW451882 N23137 N23129
35			W70051 AI038748 AA831327 AI925845 AW945895
	418056	171841_1	AA244416 AA244401
	418259	173386_1	AA807544 AA280648 AI243056 AI022744 AA705288 AA829425 AW452095 AI929317 R19039 AA282024
	418574	17590_1	AL041520 AA300086
40			AA301270 AA301379 AA301366
	419555	185884_1	AW881145 AA490718 M85637 AA304575 T06067 AA331991
	420811	196677_1	H90946 AA320597 AW954970 BE143680
	421911	208987_1	AL035633 F11794 F11783 H18042 T66089 H29379 R19493 AW134660 AI299437 AL133995 AA057405 N78357 AA917450 AI002692 T09262
	421974	209807_1	T65008 H29290 AI200874 AA894415 AI732887 AI791768 AI733447 AA988785 N62128 T09261 AW966936
	422128	211994_1	AA332215 AA403110 AW965299
45			AA343729 AA345779 AA344370
	423028	224062_1	AA495930 AI470890 H97831 AA350358 BE166712
	423476	22861_1	AA354572 AW062361 AW813419 AW816041 AI744949
50			AA366951 AA470999 AA469425
	426413	266650_1	AA377823 AW954494 AI022688
	428181	287953_1	AA423976 AA437075 BE006469
	429163	300543_1	AA884766 AW974271 AA592975 AA447312
	429540	305828_1	M85776 AA454535 AA456208 H90189
	430068	312849_1	AA464964 M85405 AA947566
55			AA465259 AW897142 AW897144
	430103	313089_1	AL133561 AL041090 AL117481 AL122069 AW439292 AI968826
	430439	31808_1	BE041395 AA491826 AA821946 AA715980 AA666102
	431089	327825_1	AA516420 C14818 C14815 C15161 C15068 D80763 D60656 AW970134 AA543007 D81004 D60184 AI498371 D60382 D60181 C15876
	431843	338324_1	AW972746 AA525323 AI150314
60			AA534222 AA632632 T81234
	432079	341114_1	AI187366 AA558869 AA618478
	432340	345248_1	NM_002959 X98248 AA233278 AA846376 AI470560 AI470533 BE327147 AW291971 AA071725 AI198417 AI365213 AI168442 AI337018
	432676	352582_2	AI475049 H85459 AA969895 AA888000 AA418326 AA418378 N71981 AL043634 AA426361 AA418275 AA232975 AL036861 BE277220 BE387505
65			N99710 AW375004 AA418268 AL079651 H85743 AW902319 AW805907 AA984366 T92310 AA405425 AA421732 AI656841 AW300968
	433075	35820_1	AW593418 T92267 BE464032 AW473548 AI359502 BE552306 AI990196 AW518351 AI239559 AW590963 AA018359 AI273737 AL042658
			AA411308 AA402810 H38111 AW013931 AW366432 AW752435 AW376124 AI292020 AI292121 AA340647 BE613672 BE409874 AA351915
			BE617026 BE019588 AW402692 AW247466 R59233 AA134761 BE254019 BE265105 D63316 BE313060 BE547713 BE536578 BE546749
			AA324185 H17386 BE253377 R87598 H29072 AA350980 BE076629 BE253957 AA532613 BE252486 AW804459 D30966 R87959 AA091632
70			BE005398 AA628622 AA994155
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	434609	38950_1	AI692552 AI393343 AI800510 AI377711 F24263 AA661876
	436023	398093_1	AI433540 AA728984 AA804981
	436716	425440_1	AI821940 N67106 AI744264 AA808846 AA643417 AA643416 Z70715
	436862	42814_2	BE514383 AA071273 AW247987 AW673286 BE312102 AW749824 BE071985 AW577383 BE071945 BE072005 AW577355 BE071965 AW239231
75			BE072000 BE071960 AW577360 AW749830 AW373020 X97303 AW995522 BE000192 BE562219 BE266655 BE264970
	437576	43892_1	AF075009 R63109 R63068
			AA827695 AA833754 AW978946
			AW502384 AI982587 AA828822
			AA947354 AA829660 AI687296
80			AW979249 D63277 AA846968
			AA868167 F21558 F31418 F35624
			H06994 BE147698

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5	441102	509604_1	AA973905 AI299888 AA917019 H63235 T90771
	442048	531432_1	AA974603 AI984319 AW340495
	443161	561305_1	AI038316 AI344631 AI261653
	444290	59994_1	AA262496 AV648929 AA305356 D61644 D78724
	444314	600667_1	AI140497 AW749625 AW749626 AW749644
10	445808	65133_1	AV655234 AW966332 AA340239
	447329	71759_1	BE090517 AW970792 AW264490 AW014985 F27436 AA947336 F15843 H89333 AA563626 F17712 BE546579 AA421821 AA284852 AA477751
	447448	722246_1	AW025245
	448150	752165_1	BE244285 C18429 H42373 AI820706 AI379786 R55439 AW276142
	448489	765247_1	AI472167 AI990315 R32175
15	448631	772996_1	AI523875 R45782 R45781
	448738	77790_1	AI554923 AI902356
	452410	9163_1	BE614081 W01988 AW500790
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			AA905453 AI204595 AW166541 AA157456 AA156269 AA383652 AA431072 AW592707 AI435410 AW272464 AI215594 AA622747 R74039
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			BE144022 BE143969 BE143915
			BE004783 BE004947 AI911790
25	452654	925931_1	BE160229 AW819879 AWB20179 AW819882 AW819876 AW820169 BE153201 AW993736 BE152911
	454775	1234106_1	AW850818 AW850833 AW851100
	455019	1249138_1	BE148152 BE148133 BE148159 BE148132 AW885107
	455272	1271871_1	BE063353 BE063955 BE063866 BE063705 BE063846 BE061416 BE063844
	455619	1346387_1	BE154075 BE153973 BE064861 BE153852 BE153847 BE064684 BE153602 BE065075 BE154018 BE064772 BE064842 BE153557 BE153509
30	455653	1348742_1	BE072092 BE072106 BE072086 BE072098 BE072103
	455729	1353792_1	BE143703 BE143631 BE143629 BE143702
	455824	1372880_1	BE162704 BE162705 BE162732 BE162702 BE162694
	455956	1387163_1	R00602 Z42921 F06132
	456123	1534442_1	M54968 NM_004985 AI808924 AL135130 AW242010 AA476848 AI740449 M17087 K03210 M35505 M35504 L00049 AI186585 W35273 X01669
35	457133	29066_1	X02825 W23635 AI554920 AI539465 AA25263 AI469981 W21091 T26976 AW977922 BE550180 AW664973 AI148939 AW117295 AA811229
			AI343010 AA766141 BE219368 N95249 AA280396 AW504574 AA232870 AI770018 AA262948 AW450230 AW362890 AW609417 AW499941
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			AI567016 N70374 AW474707 AA505084 AA082195 AW949515 AA361728 N33863 AA411821 AA401640 AW594461 AL120766 AI500024
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40			AA737010 AA872481 AA281094 AA564243 BE464958 BE049265 AW167917 AA843916 AA525301 AI015987 N25230 AI889481 AW173466
			AA937541 AI334416 AI676214 AI281159 AA553559 AA582189 AA255527 AW160515 AA670007 H08199 AA808271 AA281015 W47527 AA649252
			AI364302 AA889246 R40473 H02312 AA648116 AA342730 AA243624 R99351 R41588 R49696 AA854442 F01713 AA213685 AA721296 R79833
			H84241 R70668 H85554 AA223758 N85349 AI374913 AI306683 AA015609 AA918548 AI453570 AA772321 AI692775 AA195733 AI474563
			AW873048 AI209133 AI028182 AI374920 AW572807 AA406223 AA833684 T97255 H69138 AA382906 AW119162 N31974 AI890584 N39418
45			AA864877 AA679469 BE350651 N41020 AI050915 F00075 AA864878 N26970 AA828898 AW019991 AW796631 AW993262 N48532 BE564682
			AV654063 AI754461 AW945712 C03269 AV655314 AV659070 AV659808 AV660435 H70113 C05323 R91984 H96949 AV658936 AV658879
			H69137 AA384411 AA412584 C02749 W32014 R58168 C05526 BE536017 N24354 AA287991 N80109 F05452 R12740 H08297 AL138354
			AW020801 BE178443 BE178018 BE178336 BE178380 BE178107 BE178385 BE178215 BE178186 BE178447 BE178352 BE178422 BE178424
			BE178043 BE178093 BE178460 BE178356 BE178441 BE178438 BE178467 AI091259 BE177839 BE178094 R28455 BE177844 BE178100
50			AA262387 R70669 W80934 W93668 AA256711 BE178141 BE177893 BE178449 AA167718 H69694 BE178017 BE178029 BE177999 BE177936
			AA095144 N32462 AA281203 AA281183 W47526 W05015 R34165 R35396 T97366 R79640 W25256 R99450 AW368425 BE178196 R26447
			C03146 C03683
	457952	44256_1	U25750 AI792472 AA487379 AI872282 AA487262 R22383 AI865750 R21832 AA593628 AW571869 AA377191 R78814 T27193
	458956	83645_1	BE220675 AA345621 AA009992

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TABLE 2C

Pkey: Unique number corresponding to an Eos probeset

Ref: Sequence source. The 7 digit numbers in this column are Genbank Identifier (GI) numbers. "Dunham I. et al." refers to the publication entitled "The DNA sequence of human chromosome 22." Dunham I. et al. (1999) *Nature* 402:489-495.

Strand: Indicates DNA strand from which exons were predicted.

NL_position: Indicates nucleotide positions of predicted exons.

5				
10	Pkey	Ref	Strand	NL_position
	400481	8439853	Plus	112433-112541
	400501	9796227	Minus	12479-12619
	400713	8118874	Minus	43185-43394
	400769	8131628	Plus	28671-29795
15	400818	8569994	Plus	172644-172765,173085-173200
	400881	2842777	Minus	91446-91603,92123-92265
	400882	2842777	Minus	110431-110703
	400965	7770576	Minus	173043-173564
	400986	8085497	Minus	63140-63319
20	400995	8099094	Plus	141186-141601
	401093	8516137	Minus	22335-23166
	401178	9438616	Minus	133663-133812
	401192	9719502	Minus	69559-70101
	401209	7712287	Plus	164932-165112
25	401405	7768126	Minus	69276-69452,69548-69958
	401416	7452889	Minus	121456-121626
	401419	7452889	Minus	136389-136508
	401444	8346725	Plus	90895-90994,93070-93213
	401512	7622346	Plus	136399-136557
30	401563	8247910	Plus	91395-91763
	401600	4388746	Minus	27363-27518,28727-28891,29526-29731
	401750	9828651	Plus	82143-82270,89284-89373,90596-90770,95822-96001,96688-96775,96870-96992,98046-98138
	401757	7239630	Plus	88641-88751
	401839	7856637	Plus	1016-1086,2751-2967,3241-3348,26677-26831
35	401849	7770425	Plus	129375-129483,129597-129720
	401952	3319121	Minus	53770-53979
	401966	3126781	Plus	29397-29918
	402082	8117478	Minus	190046-190183
	402101	8117697	Plus	134308-134487,135402-135587,136421-136548
40	402106	8131652	Plus	3717-3848
	402163	8568936	Plus	166996-167119
	402185	8576002	Plus	25486-25639
	402240	7890131	Plus	104382-104527,106136-106372
	402249	7704953	Minus	107636-107813,108694-108824,110435-110502,113182-113386
45	402347	8099267	Minus	13714-15440
	402396	1905896	Plus	4426-4648
	402469	9797107	Minus	71266-72351
	402532	9800951	Minus	180240-180558
	402559	9864273	Plus	33539-33715
50	402575	9884830	Minus	109742-109883
	402602	7239666	Plus	6785-6972,7478-7575
	402758	9213869	Plus	87638-87924
	402786	9715046	Plus	47624-47795
	402807	6456148	Minus	101542-101660,103476-103656
55	402810	6010110	Plus	12715-12856,13527-13643
	402964	9581599	Minus	46624-46784
	403046	3540153	Minus	55707-55859,56369-56511
	403055	8748904	Minus	109532-110225
	403217	7630969	Plus	54089-54163,55427-55623
60	403218	7630969	Plus	58039-58149
	403291	7230870	Plus	95177-95435
	403328	8469086	Minus	120428-120703
	403654	8736093	Minus	28634-28758
	403704	4982546	Minus	8850-8996
65	403708	5705981	Minus	134394-134812
	403725	7534031	Plus	86737-86843
	403739	7630882	Plus	44563-44766,48209-48483,52255-52495
	403740	7630882	Plus	86504-87227
	403745	7652036	Minus	67610-68002
70	403746	7652036	Plus	93612-93887
	403885	7710403	Minus	53259-53524
	403893	7710581	Minus	5435-7846
	403947	7711923	Plus	38657-38817
	404039	8698763	Plus	81889-82011
75	404054	3548785	Plus	66713-69175
	404058	3548785	Plus	99397-101808
	404108	8247074	Minus	63603-64942
	404211	5006246	Plus	185728-185885,194575-194686
	404277	1834458	Minus	91665-91946
80	404384	8887028	Minus	38055-38156,42175-42391,43435-43553
	404407	7329316	Minus	48154-48499
	404489	8113772	Plus	98183-98480
	404527	8152087	Plus	127737-127796,128080-128210,129888-130054,132545-132869

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	404528	8152087	Plus	135325-135486
	404661	9797073	Plus	33374-33675,33769-34008
	404663	9797133	Plus	29885-30514
	404956	7387343	Plus	55983-56203
5	405011	6139150	Plus	117359-117612
	405044	7596797	Minus	98903-101141
	405102	8076881	Minus	120922-121296
	405109	8096886	Minus	30301-30518
	405188	6649489	Plus	134573-134678
10	405231	7249032	Minus	109793-109969
	405365	2275192	Minus	119867-120372,120481-120824,121029-121357
	405387	6587915	Minus	3769-3833,5708-5895
	405396	6624129	Minus	89965-90273
	405429	7321905	Minus	51577-51723
15	405435	7408068	Minus	51704-51841,53581-53767
	405446	7582529	Plus	99136-99313
	405503	9211311	Minus	51198-51314
	405525	9558552	Minus	19699-19828
	405529	9581957	Minus	38944-39213
20	405610	5757553	Minus	71907-72080
	405802	5924004	Minus	27743-28264
	405811	4902753	Plus	5128-5248
	406180	7283201	Minus	38923-39107
	406207	5923650	Minus	162607-162800
25	406302	8575868	Plus	168961-169150,169610-169769

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Table 3A shows the Seq ID No, Pkey, ExAccn, UnigenelD, and Unigene Title for all of the sequences in Table 4.

Pkey: Unique Eos probaset identifier number

ExAccn: Exemplar Accession number, Genbank accession number

UnigenelD: Unigene number

Unigene Title: Unigene gene title

Seq ID No: Seq ID number correlation for those sequences in Table 4

	Pkey	ExAccn	UnigenelD	Unigene Title	Seq ID No
10	415539	AI733881	Hs.72472	BMP-R1B	Seq ID No 1 & 2
	448988	Y09763	Hs.22785	gamma-aminobutyric acid (GABA) A recepto	Seq ID No 3-10
	403740			NM_001076*:Homo sapiens UDP glycosyltran	Seq ID No 11 & 12
	408633	AW963372	Hs.46677	PRO2000 protein	Seq ID No 13 & 14
	408660	AA525775		ESTs, Moderately similar to PC4259 ferri	Seq ID No 15 & 16
15	409051	AA080912		gb:zn04d03.r1 Stratagene hNT neuron (937	Seq ID No 17
	409123	AA063403		gb:zm04d12.s1 Stratagene corneal stroma	Seq ID No 18
	415787	H01463	Hs.93534	ESTs	Seq ID No 19-21
	415999	AA172179	Hs.294029	ESTs	Seq ID No 22
	416225	AA577730	Hs.188684	ESTs, Weakly similar to PC4259 ferritin	Seq ID No 23
20	420757	X78592	Hs.99915	androgen receptor (dihydrotestosterone r	Seq ID No 24 & 25
	429163	AA884766		gb:am20a10.s1 Soares_NFL_T_GBC_S1 Homo s	Seq ID No 26
	429441	AJ224172	Hs.204096	lipophilin B (uteroglobin family member)	Seq ID No 27 & 28
	431099	Y13367	Hs.249235	phosphoinositide-3-kinase, class 2, alph	Seq ID No 29 & 30
	432432	AA541323	Hs.115831	ESTs	Seq ID No 31
25	432435	BE218886	Hs.282070	ESTs	Seq ID No 32 & 33
	432527	AW975028	Hs.102754	ESTs	Seq ID No 34
	435876	AW612586	Hs.160271	G protein-coupled receptor 48	Seq ID No 35 & 36
	438233	W52448	Hs.56147	ESTs	Seq ID No 37-40
	439569	AW602166	Hs.222399	CEGP1 protein	Seq ID No 41 & 42
30	440819	AI809444	Hs.202108	ESTs	Seq ID No 43
	442832	AW206560	Hs.253569	ESTs	Seq ID No 44
	447342	AI199268	Hs.19322	Homo sapiens, Similar to RIKEN cDNA 2010	Seq ID No 45 & 46
	447499	AW262580	Hs.147674	protocadherin beta 16	Seq ID No 47 & 48
	451411	AA017492	Hs.135655	EST	Seq ID No 49
35	451720	AW970985	Hs.290853	ESTs	Seq ID No 50 & 51

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Table 3B shows the accession numbers for those Pkey's lacking UnigenelD's for table 3A. For each probeset is listed gene cluster number from which oligonucleotides were designed. Gene clusters were compiled using sequences derived from Genbank ESTs and mRNAs. These sequences were clustered based on sequence similarity using Clustering and Alignment Tools (DoubleTwist, Oakland California). Genbank accession numbers for sequences comprising each cluster are listed in the "Accession" column.

5	Pkey	CAT Number	Accession
	408660	107294_1	AA525775 AA056342 AI538978 AW975281 AA664986
	409051	109699_1	AA080912 AA075318 AA083403 AA076594 AA078992 AA084926 AAC81881 AA113913 AA113892 AA083821 AA134801 AA082953 AA070343
			AA062835 AA075419 AA063293 AA071252 AA078900 AA062836 AW974305
	409123	110143_1	AA063403 AA070823 AA070050
10	429163	300543_1	AA884766 AW974271 AA692975 AA447312

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Table 3C shows genomic positioning for those Pkey's lacking Unigene ID's and accession numbers in table 3A. For each predicted exon is listed genomic sequence source used for prediction. Nucleotide locations of each predicted exon are also listed.

5	Pkey 403740	Ref 7630882	Strand Plus	Nt_position 86504-87227
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Table 4:

Seq ID NO: 1 DNA sequence
Nucleic Acid Accession #: NM_001203
Coding sequence: 274..1782

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5      1      11      21      31      41      51
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10    CGCGGCGCGC GGAGCTCGCG GGGCCTCGCG GGACGCGGCG AGTGCAGAGA CCGCGGCGCT 60
      GAGGACGCGG GAGCGGGGAG CGCACGCGCG GGTGGAGTT CAGCCTACTC TTCTTAGAT 120
      GTGAAAGGAA AGGAAGATCA TTTCATGCCT TGTGATAAAA GGTTTCAGACT TCTGCTGATT 180
      CATAACCATT TGGCTCTGAG CTATGACAAG AGAGGAAACA AAAAGTTAAA CTTACAAGCC 240
      TGCCATAAGT GAGAAGCAAA CTTCCTTGAT AACATGCTTT TGGGAAGTGC AGGAAAATTA 300
      AATGTGGGCA CCAAGAAAGA GGATGGTGAG AGTACAGCCC CCACCCCCCG TCCAAAGGTC 360
15    TTGGTGTGTA AATGCCACCA CCATTGTCCA GAAGACTCAG TCAACAATAT TTGCAGCACA 420
      GACCGATATT GTTTCACGAT GATAGAAGAG GATGACTCTG GGTTCCTGT GGTCACTTCT 480
      GGTGCTCTAG GACTAGAAGC CTCAGATTTT CAGTGTCTGG ACACCTCCAT TCCTCATCAA 540
      AGAAGATCAA TTGAATGCTG CACAGAAAGG AACGAATGTA ATAAAGACCT ACACCTTACA 600
      CTGCTCCCAT TGAAAAACAG AGATTTTGTG GATGGACCTA TACACCACAG GGCTTTACTT 660
20    ATATCTGTGA CTGTCTGTAG TTGCTCTTG GTCCCTATCA TATTATTTTG TTACTTCCGG 720
      TATAAAGACG AAGAAACACG ACCTCGATAC AGCATTGGGT TAGAACAGCA TGAACCTTAC 780
      ATTCTCTCTG GAGAATCCCT GAGAGACTTA ATTGAGCAGT CTCAGAGCTC AGGAAGTGGA 840
      TCAGGCTCTC CTCTGCTGGT CCAAGGAGCT ATAGCTAAGC AGATTTCAGT GGTGAAACAG 900
      ATTGGAAAAG GTCCGCTATGG GGAAGTTTGG ATGGGAAAGT GCCTGGGCGA AAAGGTAGCT 960
25    GTGAAAGTGT TCTTCACCAC AGAGGAAGCC AGCTGTTTCA GAGACACAGA AATATATCAG 1020
      ACAGTGTGTA TGAGGCATGA AAACATTTTG GGTTCATTG CTGCAGATAT CAAAGGGACA 1080
      GGTCTCTGGA CCCAGTTGTA CCTAATCACA GACTATCATG AAAATGGTTC CCTTTATGAT 1140
      TATCTGAAGT CCACACCCCT AGACGCTAAA TCAATGCTGA AGTTAGCCTA CTCTTCTGTC 1200
      AGTGGCTTAT GTGCTTATCA CACAGAAATC TTAGTACTC AAGGCCAACC AGCAATTGCC 1260
30    CATCGAGATC TGAAAAAGTA AAACATTTCT GTGAAGAAAA ATGGAAGTTC CTCTATTGCT 1320
      GACCTGGGCC TGGCTGTGTA ATTTATTAGT GATACAAATG AAGTTGACAT ACCACCTAAC 1380
      ACTCGAGTTG GCACCAACCG CTATATGCCT CCAGAAAGTGT TGGACGAGAG CTGGAACAGA 1440
      AATCACTTCC AGTCTTACAT CATGGCTGAC ATGTATAGTT TTGGCCTCAT CCTTTGGGAG 1500
      GTTCTAGGTA GATGTGATC AGGAGGTATA GTGGAAGAA ACCAGCTTCC TTATCATGAC 1560
35    CTAGTGCCCA GTGACCCCTC TTATGAGGAC ATGAGGGAGA TTGTGTGCAT CAAGAAGTTA 1620
      CGCCCTCAT TCCCAAAACG GTGGAGCAGT GATGAGTGT TAAGGCAGAT GGGAAAACCTC 1680
      ATGACAGAA GTCTGGGCTCA CAATCCTGCA TCAAGGCTGA CAGCCCTGCG GGTAAAGAAA 1740
      ACACCTGCCA AAATGTGAGA GTCCACAGAC ATTAACTCT GATAGGAGAG GAAAAGTAAG 1800
      CATCTCTGCA GAAACCCAAC AGCTACTCTT CTGTTTGTGC CCAGACCAA AGACATCAA 1860
40    TAAGCATCCA CAGTCAAGC CTGGAACATC GTCCCTGCTC CAGTGGGTT CAGACCTCAC 1920
      CTTTCAGGGA GCGACCTGGG CAAAGACAGA GAAGCTCCCA GAAGGAGAGA TTGATCCGTG 1980
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Seq ID NO: 2 Protein sequence
Protein Accession #: NP_001194

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      DSGLPVVTSG CLGLEGSDFQ CRDTPIPHQR RSIECCTERN ECNKDLHPTL PPLKNRDFVD 120
      GPIHHRALLI SVTVCSLLLV LIILFCYFRY KRQETRPYS IGLEQDETYI PPGESLRDLI 180
      EQSGSGSGSG GLPLLVQRTI AKQIQMVKQI GKGRYGEVMM GKWRGEKVAV KVFETTEBAS 240
      WPRETEIYQT VLMRHENILG FIAADIKGTG SWTQLYLITD YHENGSLYDY LKSTTLDAKS 300
      MLKLAYSSYS GLCHLHTEIF STQGKPAIAH RDLKSKNILV KKNGTCCIAH LGLAVKFISD 360
55    TNEVDIPNPT RVGTCRYPMP EVLDESLNRN HFQSYIMADM YSFLILWEV ARRCVSGGIV 420
      BEYQLPYHDL VPSDPSYEDM REIVCIKKLR PSFPNRWSSD ECLRQMGKLM TECWAENPAS 480
      RLTLALRVKKT LAKMSBSQDI KL

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Seq ID NO: 3 DNA sequence
Nucleic Acid Accession #: NM_004961.2
Coding sequence: 55..1575

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      CCTCAGACTG AATCAAGAA TGAAGCCTCT TCCCGTGATG TTGCTATGAG CCCCAGGCC 180
      CAGCCTCTGG AAAATCAGCT CCTCTCTGAG GAAACAAAGT CAACTGAGAC TGAGATCGGG 240
      AGCAGAGTTG GCAAACTGCC AGAAGCCTCT CGCATCTCTG ACACTATCCT GAGTAATTAT 300
70    GACCACAAAC TGCGCCCTGG CATTGGAGAG AAGCCCACTG TGGTCACTGT TGAGATCGCC 360
      GTCAACAGCC TTGCTCTCTC CTCTATCCTA GACATGGAAT ACACCATGTA CATCATCTTC 420
      TCCAGACCTT GGTACGACGA ACGCTCTGTG TACAACGACA CCTTTGAGTC TCTTGTCTTG 480
      AATGGCAATG TGGTGGAGCA GCTATGGATC CCGGACACCT TTTTATAGGA TTCTAAGAGG 540
      ACCCAGCAGC ATGAGATCAC CATGCCAAC CAGATGGTCC GCATCTACAA GGATGGCAAG 600
75    GTGTTGTACA CAATTAGGAT GACCATTGAT GCCGATGCT CACTCCACAT GTCAGATT 660
      CCAATGGATT CTCACTCTTG CCCTCTATCT TTCTCTAGCT TTTCTATACC TGAGAAATGAG 720
      ATGATCTACA AGTGGGAAAA TTCAAGCTT GAAATCAATG AGAAGAACTC CTGGAAGCTC 780
      TTCCAGTTTG ATTTTACAGG AGTGAGCAAC AAAACTGAAA TAATCACACA CCCAGTTGGT 840
      GACTTCATGG TCATGACGAT TTCTTCAAT GTGAGCAGGC GGTTTGGCTA TGTGCTCTT 900
80    CAAAATATG TCCCTTCTTC CGTGACCACG ATGCTCTCCT GGGTTTCTCT TTGGATCAAG 960
      ACAGAGTCTG CTCCAGCCCG GACCTCTCTA GGGATCACCT CTGTTCTGAC CATGACCACG 1020
      TTGGGCACTT TTTCTCTGTA GAATTTCCCG CGTGTCTCCT ATATCACAGC CTGGAATTTC 1080
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Protein Accession #: NP_004952.1

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IFSGTWYDER LCYNDFESL VLNGNVVSQL WIPDTFFRNS KRTHBEHEIM PNQMVRIYKD 180
GKVLVITRMT IDAGCSLHML RFPMDSHSCP LSFSSFSYPE NEMIKWENF KLEINEKNSW 240
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IKTESAPART SLGTSVLMT TTLGTFSRKN FPRVSYITL DFYIAICFVF CFCALLEFAV 360
LNFLLIYNQTK AHASPKLRHP RINSRAHART RARSACARQ HQBAFVCQIV TTEGSDGBER 420
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Coding sequence: 572..1753

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GTGTAAAGAA AGCCAAATCA AGGACCCGAA TGTGAGCAGG ACCTCAGAAG CCCCCTTTGT 240
CACTGCTCTC CAGCAAAAGC AGCACTATCC GGACTTCTAA CACCATCGGG TCGAGGGACC 300
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GCCCTCTGAA AATCAGCTCC TCTCTGAGGA AACAAAGTCA ACTGAGACTG AGACTGGGAG 420
CAGAGTTGGC AAATGCGCAG AAGCCTCTCG CATCTGAAC ACTATCTGTA GTAATTATGA 480
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Protein Accession #: NP_068819.1

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 LSWVSFWIKT ESAPARTSLG ITSVLMTTL GTFSRKNFPR VSYITALDFY IAICFVFCFC 240
 ALLEFAVLNF LIYNQTKAHA SPKLRHPRIN SRAHARTRAR SRACARQHQE AFVCQIVTTE 300
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Nucleic Acid Accession #: NM_021987.1
Coding sequence: 572..1657

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Seq ID NO: 8 Protein sequence
Protein Accession #: NP_068822.1

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Seq ID NO: 9 DNA sequence
Nucleic Acid Accession #: NM_021990.1
Coding sequence: 1309..2490

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Seq ID NO: 10 Protein sequence
 Protein Accession #: NP_068830.1

30 1 11 21 31 41 51
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 35 LSWVSFWIKT ESAPARTSLG ITSVLMTTL GTFSRKNFPR VSYITALDFY IACIFVFCFC 240
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 Coding sequence: 22..1614

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Seq ID NO: 12 Protein sequence
 Protein Accession #: NP_001067.1

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PCT/US02/17594

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    YDYSNKLCKD AVLNKKLMMK LQBSKFDVIL ADALNPGCEL LAELFNIPFL YSLRFSVGYT 180
    FEKNGGGFLF PFSYVPVVMs ELSDQMIFME RIKNMIHMLY FDFWFIQYDL KKWDFYSEV 240
    LGRPTTLFET MGKAEMLLIR TYWDFEFPRP FLPNVDFVGG LHCKPAKPLP KEMEEFVQSS 300
10  GENGIUVFSL GSMISNMSBB SANMIASALA QIPQKVLNRF DGKPKNTLGS NTRLYKWLPQ 360
    NDLLGHPKTK AFITHGGTNG IYBAIYHGIP MVGIPLFADQ HDNIAHMKAK GAALSVDIRT 420
    MSSRDLLNAL KSVINDPVYK ENVMKLSRIH HDQPMKPLDR AVFWIEFVMR HKGAKHLRVA 480
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Seq ID NO: 13 DNA sequence
Nucleic Acid Accession #: NM_014109.1
Coding sequence: 551..1739

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    CACTTAAAGC CACATTTACC ACATTATTAC AGAATATTCC TTCATTIGCT CCAGTTTATC 240
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25  TCCGTGATTA TGGAGAGATT TTTAATGTCC AGTTACCGGA TAAAGAAGAA CGGACAAAAT 360
    TTTTGAAGA TTTAATTCTA AAAAAGCTG CTAAGCCTCC TATATCAAAA AAGAAGACAG 420
    TTTTGCAGGC TTTGGAGGTA CTCCCAGTAG CACCACCACC TGAGCCAAGA TCACTGACAG 480
    CAGAGAAGT GAACGAGCTA GAAGAACAAG AAGAAGATAC ATTTAGAGAA CTGAGGATTT 540
    TCTTAAGAAC TGTACACAT AGGCTTGCTA TTGACAAGCG ATTCCGAGTG TTTACTAAGC 600
30  CTGTTGACCC TGAAGAGGTT CCTGATTATG TCACTGTAAT AAAGCAACCA ATGGACCTTT 660
    CATCTGTAAT CAGTAAATTT GATCTACACA AGTATCTGAC TGTGAAAGAC TATTTGAGAG 720
    ATATTGATCT AATCTGTAGT AATGCCITAG AATACAATCC AGATAGAGAT CCTGGAGATC 780
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    AACTTGATGA AGACTTTGAG CAGCTCTGTG AAGAAATTCG GCAATCTAGA AAGAAAAGAG 900
35  GTTGTAGCTC CTCCAAATAT GCCCCGCTCT ACTACCATGT GATGCCAAG CAAATTTCCA 960
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    CTCCTGTGGC TGCAGCACT CTGCTCAGT TGAAGAGGAA AATTGCGAAA AAGTCAAACT 1080
    GGTACTTAGG CACCATAAAA AAGCGAAGGA AGATTTCACA GGCAAGGAT GATAGCCAGA 1140
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    AAACATCACT TATTCAGAAA ATGGAGCAAG AGGTAGAAAA CTTCACTGTG TCCAGATGAT 1740
    GATGTCTATG TATCAGTAT TCTTTATATT CAGTTCCTAT TTAAGTCATT TTGTCTATG 1800
50  CCGCTTAATT GATGTAGTAT GAAACCTGTC ATCTTTAAGG AAAAGATTAA AATAGTAAAA 1860
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Seq ID NO: 14 Protein sequence
Protein Accession #: NP_054828.1

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    TFPSTPVACST PAQLKRKIRK KSNWYLGTIK KRRKISQAKD DSQNAIDHKI BSTDTEBTQDT 180
    SVDHNETGNT GESSVEENEK QQNASESKLE LRNNSTNCNI ENELEDSRKT TACTELRDKI 240
    ACNGDASSSQ IHIHSDENEG KEMCVLRMTR ARRSQVEQQQ LITVEKALAI LSQPTPSLVV 300
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Seq ID NO: 15 DNA sequence
Nucleic Acid Accession #: AK001536

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75  CTCAAAAACC TTACCCAGGT TATGCTACCA AACAAAAACT TGCTTTAGCA ATCAATGCAG 240
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    TTTCAAAATA GAGAAGCCAG ATGGTGTGTT ACCACCTATA GCACCTTTCA ATTACACACA 420
    ATCATCCATG CATTATGAA AAACCCATAC CCTGGGATTG ATTCGGGAGA ACAACTTGCT 480
80  GAAGAAATGG GTGCTTCAGA GTCAAGAGTC CAAATTGGT TCCAAAATCA AAGATCTAGA 540
    TTTTATCTCC AGAGAAAAG AGAACCTGTT ATGTCTTAG AATGAGAAGA CCAGAGAAGA 600
    CCAGGGGCAA GGTTTCTGAG GGACTTCAAG GTACAGAAGA TACACAAAGT GGCACCAGCC 660
    TCACTAGCAC TCTCATTTCT CAAGAGCCAG AACATGGTGA ATACAGTCAA GTTCAGTGTA 720

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TGTCTTAAAT TTTAAACTC TTGATGCTGG CTGGGTTCCG TGGCTCATAC CTGTAAATCC 2280
ATCACTTTGG GAGGCCAAGA CAGGTTGATT ACTTGAATTC AGGAGTTCAA GACCAGCTCG 2340
GACACATGG CAAACACGT CTTAAAAAA AGAAAAAGAA AAAGAAAAAC AGAAAGAAAA 2400
AGAAGAAAA CTACTTGCTG CCTTACTTG AAGCTCAATT ATTTAAAAA

Seq ID NO: 16 DNA sequence
Nucleic Acid Accession #: CAT cluster

35
40
45

1 11 21 31 41 51
CTTTTTTTTT TTTTTTTTTT TAGTAGAGAC AGGGTTTCAC CATGTTAGCC AGGATGGTCT 60
CGATCTCCTG ACCTCATGAT CTTCTGCTT TGGCCTCCCA AAGTGCTGCG ATTACAGGCG 120
TGAGCCACTG CACCCAGCCC AGAGTTTTTT TTAACAAGGT TCTTCTCAGC AATTCTAGTA 180
TCCAGATATA GGCCCATCAT AGACATCACA CAAGCGTGTA CTTTATAATC CTGGTGAATA 240
CAGAAGTTTC CTGGACTCCT TGATGAGCTA CTGCTTTCGC TCCTATATCA GTGTTTTCAG 300
CTGATGTCAT TTGTGATTGT GTTTCGACT TTCTGTAGGC AGAAAAAACC TTTTCAATTTT 360
TTTTTGCTTA CATGCACATA AATGTAAGCG CTAATTCTTA TATTAACTG TTTATTCTTA 420
TAATACTTAA TTGGCTGTTT TCCTGGCTGA ACCAAACCAA GAGCATAAGG AATGATAACC 480
TTCAAACTG ATTAAATTAG AGATCAATAA ATGGAGCTGT TTAAATCTTA TTATCTTCT 540
TTCATAGATT AAATAGAAAA TTTTT

Seq ID NO: 17 DNA sequence
Nucleic Acid Accession #: CAT cluster

50
55
60

1 11 21 31 41 51
GGCAGGAGAA GACGCCACAT CCCCTATTAT AGAAGAGCTA ATAAATTTCC ATGATCACAC 60
ACTAATAATT GTTTTCTCTA TTAGCTCCTT AGTCTCTAT ATCATCTCGC TAATATTAAAC 120
AACAAACTA ACACATACAA GCACAAATAGA TGACAAAGAA GTTGAAACCA TTTGAACTAT 180
TCTACAGCT GTAATCCTTA TCATAATTGC TCTCCCTCT CTACGCATTC TATATATAAT 240
AGACGAAATC AACACCCCG TATTAACCGT TAAACCATTA GGGCACCAAT GATACTGAAG 300
CTAGCAATAT ACTGACTATG AAGACCTATG CTTTGATTCA TATATAATCC CAAACAAACGA 360
CCTAAACCTT GGTGAACACT GACTGCTAGA AGTTGATAAC CGAGTCTGTC TGCCAAATAGA 420
ACTTCCAATC CGTATATTAA TTTCACTGTA AGACGTCCTC CACTCATGAG CAGTCCCCTC 480
CCTAGCACTT AAAACTGATG CCATCCCAGG CCGACTAAAT CCAGCAGAGT ACATCAACCG 540
ACCAAGGGTTA TTTATGCGCC AATGCTCTGAA TTTGTGGTCT TACCATAGCT TTTTGCCATT 600
GTCTAGAAAT GGGTCCCTAA AATATTTCGG NACTGGTCTG

Seq ID NO: 18 DNA sequence
Nucleic Acid Accession #: CAT cluster

65
70
75
80

1 11 21 31 41 51
GTGTACATCA GAGCAAAAT ACAGAGTATT TATTCAITTC TTCCCACTAG AGGGACACAC 60
TGTTCTTGGA CAGACAAATC AATCATCAGT TGTGAGGAGT TGCCCTTTGGA GAATGATCAA 120
TGAACCTCTT TTCAGGGGTT GGAAATTGAT ACCAGGGTCC ATCACTTCGG GCACGCATCA 180
GCCTTGAAC TTCTGCTCC TTTAACCGTA ACTCAGCCTT TTCAGATTCA ATCTGGAGGA 240
TAGCCAGGCT TTCTCTGTA TTTCTTTTCA GGCATCATA GAAATTCGGG GCGATCCATC 300
TTGATATCGG ATGCTTGTAA TACTCCAGT GTTCAGGGAT GTAGCCTTCT GGGATTCTCTG 360
CAAGCTCGGC TTCACCAATA AATATGTTCA CCAGTGTAT GCCAATTATA ACTGGGATCC 420
CAGTCAACTC AAGGTAGAA TTTCTTAAAC TCAAGAAGCG AGCGTCATAG TATAAAGAG 480
GCTTGACGAC AAACAGTCTC TTGCCATGTC CCACCTGTGC CGCACAGGAG CGACAGTCTT 540
CGGAANTCC GCGTGAGAAA ACTTCCGACT CCGAGTCTAG GACCAGCGCG GCGGCAAGAC 600
CACGCTGTCA GCGCGGAGAC CGAANCCGCT GCAGCAGCTC ATGGCCGCCA TGG

Seq ID NO: 19 DNA sequence
Nucleic Acid Accession #: CAT cluster

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PCT/US02/17594

1 11 21 31 41 51
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 TAGTCCAGTN AATTACTTTA ATTTGCTTT TCCATAATAC TGGTATTCCA TAGAAGAAAA 60
 TCTTTTATTA ATATTCTATA CTACTACATC CGACACCAGA TGAATAAGT TTGCAATGGT 120
 CCAAAATTC GTAAACCCAT TAAATGCAAT TCATACTTTA TTTTGGCAGT ATTCATTTC A 180
 TCATTACTTT ATTTGGATGC TAACGCAAGT ACTTCTAAGG AAAAGCTGTC ATATAATTAC 240
 TTTAGTCAAG CATTAGTAG AGGCAATAAT CAAACCTCTA TCCCAACATT TTACACTTGT 300
 AACAGAATGA AGGATGAGGT ACAACATACA TTTTGGCAA TTTACTATTA AGGGCCATAA 360
 TCATTTTAGG GGCCTTAGG GCCCATATAT ATATAATAT ATTTTGGAC A

Seq ID NO: 20 DNA sequence
 Nucleic Acid Accession #: U92072
 Coding sequence: 351..3701

1 11 21 31 41 51
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 CGGGTCATGG ATCGCGCGGC AGCGCGCGCG GACGCGCGGA GCCCGGCCGC GACCAGGTGA 120
 GGAGGCGCGC TCCGGCGCCA CTGCAGCCGC AGCGGCTCG GAGGAAGAGG GCTCGCGGCC 180
 GCGCGCGCGC CGCGCGTCCG TGCCCTTCTT GTTGGGATTA TCTTCTGCTC CCCGCTGCTT 240
 CTTGCTCTCC CGCGCTCGAA GCGGCTCTTA GGCTTCAGCG GCTCGGACTC CTGGGCAGCC 300
 GGTGCTCTG CTACCTGGGC CTGCTAGCTG GGAGACCCTT GGGCGAGACC ATGAGGAAT 360
 TCAACATCAG GAAGGTGCTG GACGCGCTGA CCGCAGGCTC GTCCCTCGGCC TCGCAACAGC 420
 AGCAACAGCA GCACGACCCG CCTGGGAACC GGGAGCCCGA GATCCAGGAG ACGCTCCAGT 480
 CCGAGCACTT CCAACTCTGC AAGACTGTTC GCCATGGATT TCCCTATCAG CCCTCAGCCC 540
 TGGCCTTTGA TCCGTTTCAG AAGATCCTGG CGGTAGGAAC CCAGACTGGT GCTTTAAGGC 600
 TCTTTGGTGC TCCAGGGGTG GAATGTTATT GCCAGCACGA CAGCGGAGCG GCAGTGATTG 660
 AACTCCAGTT CCTGATTAAAT GAGGGAGCCC TTGTGAGTGC CTTGGCTGAT GACACCTTAC 720
 ACTTGTGGAA GTCAAGTCAG AAAAGCGCTG CTGTGCTACA TTCACTCAAA TTTTGCAGAG 780
 AAAGGGTTAC ATTTTGCCAT CTGCCTTTCC AGAGTAAGTG GCTCTATGTG GGCACGGAAC 840
 GAGGTAATAT ACATATTGTC AATGTGGAGT CCTTCACACT CTCAGGCTAC GTCATTATGT 900
 GGAATAAAGC CATCGAACTG TCATCTAAAT CTCACCCAGG ACCTGTTGTC CATATAAGTG 960
 ATAATCCCAT GGAGCGAGGG AAGCTTCTGA TTGGCTTTGA ATCTGGAACA GTAGTCTTAT 1020
 GGGACCTTAA GTCAAGGAAG GCTGACTACA GATACACTTA CGACGAGGCT ATTCAGCTG 1080
 TGGCTTGGCA TCATGAAGGA AAAAGTTTAT TTGTCAGTCA TTCTGATGGT ACATTGACCA 1140
 TATGGAATGT GAGTGCCCC ACTAAACCTG TACAGACCAT CACTCCTCAC GGAAAAAGT 1200
 TAAAGGATGG GAAGAAACCC GAGCCGTGCA AGCCTATCCT CAAGGTGGAG TTCAAGACAA 1260
 CAAGATCGGG GGAACCTTTT ATTATTTTGT CGGGAGGCTT ATCATATGAT ACCGTGGGAA 1320
 GAAGACCTTG CTTAACAGTG ATGCATGGGA AAAGCACGGC AGTGCTGGAA ATGGAATATT 1380
 CAATTGTCCA CTTTCTCACA CTCTGTGAAA CGCCATATCC AATGATTTT CAGGAGCCGT 1440
 ATGCTGTGGT TGTCTCTCTG GAGAAGGATT TAGTGCTGAT AGACCTGGCA CAGAATGGAT 1500
 ACCCTATATT TGAGAATCCC TACCCTTTGA GTATACACGA GTCCCTGTTT ACATGTTGTG 1560
 AATATTTTGC TGATGTCTCT GTGGACCTTA TTCTCTGACT TTATTTCTGT GGAGCTAGAC 1620
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 GTGCTCAAAG TTACCCAGAA ATAATTATTA CAGGGCATGC TGATGGCTCA ATTAAATTCT 1740
 GGGATGCTTC TGCAATAACT CTACAAGTAC TGTATAAAT AAAAACATCT AAAGTATTTG 1800
 AAAAGTCAAG AATATAAGAT GACAGACAGA ACACCGACAT TGTAGATGAA GATCCATATG 1860
 CCATTGAGAT CATCTCTCGG TGCCACAGAGA GCAGAAATGCT GTGCATAGCC GGAGTGTCCG 1920
 CTCATGTCTC CATTATATGA TTCAGCAAGC AGGAAGTGGT TACAGAAGTC ATCCGATGTC 1980
 TTGAAGTCCG ACTGTTATAT GAAATAAATG ATGTGGAAC GCCGAGGGT GAGCAGCCAC 2040
 CCCCTTTGTC CACTCCCGTG GGCAGCTCCA CCTCTCAGCC CATCCCCCTT CAGTCTCATC 2100
 CGTCTACCGA CAGCAGCTCA TCGGACGGGC TTCCAGATAA TGTACCGTGT TTAAGAGTTA 2160
 AAAACTCACC ACTTAAACAG TCTCCCGCT ATCAAACAGA GCTAGTCATC CAGTTGGTGT 2220
 GGGTGGGTGG AGAACCOCCT CAGCAGATCA CCAGCCTAGC ACTCAACTCT TCCTACGGAT 2280
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 GGTGCCCCG CAAATCTCGA CAGCCTTCAG GAGCGGGCTT GTGTGATATT ACCGAAGGAA 2460
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 TGAGAATGGC ATTTCTGGAT GCGCGGGCT GCTTAATGCC ACCTGCATAC GAACCTTGA 2880
 CAGAGCACAA CGTTCCTGAA GAAAAAGACG AAAAGGAGAA ATTGAAAAAG CGGCGACCTG 2940
 TCTCAGTGT CCCCCTCTCT TCTCAGGAAA TTAGTGAAAA CCAGTACGCA GTGATATGTT 3000
 CTGAAAAGCA AGCAAAGTCT ATCTCCTGTC CAACCCAGAA CTGTGCATAC AAGCAGAA 3060
 TCACTGAGAC GTCTTCTGTC CTCCGTGGAG ACATTGTGCG CCTGAGTAAC AGTGTCTGCC 3120
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 TGCTGCTGAT GTACTACCTG CCCCCTACCA ACATGCGGAT AGCCAGGACA TTCTGCTTCG 3240
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 GTCAGGAGAC GTGTGAAAC CTTCAGGAGA TGCTTGGTGA GCTCTTCACC CCTGTAGAAA 3360
 CACCAGAAAG ACCAAACAGA GGGTTCTTCA AAGGCTTATT TGGAGGTGGT GCACAAATCT 3420
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 AGCACATCC GGGTCTGGC GGGATCGAAG GTGTGAAGGG AGCCGCTCG GAGTGGTGG 3540
 GAGAACTGGC CCGAGCCAGG CTGGCCCTCG ACGAAAGAGG ACGAAGCTC AGCAGCTTGG 3600
 AAGAGAGGAC TGCAGCCATG ATGTCCAGTG CAGACTCGTT TTCCAAACAT GCTCATGAGA 3660
 TGATGCTGAA ATACAAAGAT AAGAAAGTGT ACCAGTCTCG ACAAGTAGCA CTCAGTAAGT 3720
 CCAGCTTCAA CCAGAAAGAA AAAGACGTTT CCTTGTGTG GTCACTGATG TATTTGGGAA 3780
 AGATAACATA AAAGGATGTC ACAGTCTGTA CAGCGTCTTT CCCAGCACAA TCATGCACTT

Seq ID NO: 21 Protein sequence
 Protein Accession #: AAD04756

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PCT/US02/17594

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1      11      21      31      41      51
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5  MRKFNIRKVL DGLTAGSSSA SQQQQQQHP PGNREPEIQE TLQSEHFQIC KTVRHGFPYQ 60
PSALAFDPVQ KILAVGTQTG ALRLFGRRPGV EYCOQHDSCA AVIQLQFLIN EGALVSALAD 120
DTLHLWNLRQ KRPAVLHSLK FCRERVTFCH LPFOQKWLIV GTERGNIHIV NVESFTLSGY 180
VIMWNKAIEL SSKSHPGPVV HISDNPMDEG KLLIGFESGT VVLWDLKSKK ADYRYTYDEA 240
IHSVAMHHEG KQFICSHSDG TLTINWVRSP TKPVQITTPH GKQLKDGKKP EPCKPILKVE 300
FKTTRSGEPF IILSGGLSYD TVGRRPCLTV MHGKSTAVLE MDYSIVDFLT LCETTPYPNDF 360
10 QEPYAVVULL EKDLVLLDLA QNGYPIFENP YPLSIHESPV TCCEYFADCP VDLIPALYSV 420
GARQKRGYS KKEWFINGGN WGLGAQSYPE IITGHADGS IKFWDASAIT LQVLYKLKTS 480
KVFEKSRNKD DRQNTDIVDE DPYAIQIISW CPESRMLCIA GVSANVYYR FSKQEVVTEV 540
IPMLEVRLLY EINDVETPEG EQPPPLSTPV GSSTSQPIPP QSHPTSTSSS SDGLRDNVPC 600
LKVKNSPLKQ SPGYCTELVI QLVWVGGEPP QOITSLALNS SYGLNVFGNS NGIAMVDYLO 660
15 KAVLLNLSTI ELYGSDPYR REPRSPRKS RPSGAGLCDI TEGTVVPEDR CKSPTSAMKS 720
RKLSLPTDLK PDLDVKNDSF SRSRSSSVTS IDKESREAIS ALHFCETFTK KADSSPSPCL 780
WVGTTVTGAF VITLNLPLGP EORLLQPVIV SPSGTILRLK GAILRMAFLD AAGCLMPPAY 840
EPWTEHNVP EKDKEKELKK RRPVSVSPSS SQEISENQYA VICSEKQAKV ISLPTQNCAY 900
KQNHTEFSV LRGDIVALS SVCLACFCAN GHIMTFSLPS LRPLLDVYYL PLTNMRIART 960
20 PCFANSQOAL YLVSETIQR LTYSOETCEN LOEMLGELEF PVETPEAPNR GPFKGLFGGG 1020
AQSLDREELF GESSSGKASR SLAQHIPGPG GIEGVKGAAS GUVGELARAR LALDERGQKL 1080
SDLEERTAM MSSADSFSKH AHEMMLKYKD KKWYQF

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Seq ID NO: 22 DNA sequence
Nucleic Acid Accession #: CAT cluster

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1      11      21      31      41      51
|      |      |      |      |      |
30 TCCCATCGGG TGAACCGTGG TCTTGTTCCG TCGGCCACCA ATCGCTCTCC AGCTTGACG 60
GCCCCGCGCA AGCCTGGCTC GTTCACAGCT CTCTCGCACC TCCTGGAGCT TCAGCTTCTT 120
CCGTTGCAAG GAAGCTTTAT GGGCCAATTC GTTCGGCACC CCGGGGGCAG GTGCGCGGTG 180
CGCGGGGAGG AAGAGGATTT GACTGCGGTT TCCACCCCCC GCGGCCCAAC CTCACCCCG 240
GTGCGCGCGC TCTTCCAGGC TCCTGCTGGT CCCACTTGCC AGGAGTTAGG TCTCAGGTCA 300
35 GCCTGAGCTC CTGACAGGCC CAGGCCCGGA AAGACACGTA GGGGAACCA TCTGCTCACT 360
TCTGTCTCTG CCGGAAGGGA TCCCTTTCTG ACGGGAAGA AAGGCGCTAA ACAAGCAGTG 420
GCCTTGAGAT AAGCAATGCT GAAGCACTTG CAGCTCACTT ATTACCATAA ACTGACTGAG 480
CCCTCCCTAC ACAAGCCGTA ACTACTGCTT TGATTGGACA AGAGACTGAT TTCAGTAGTT 540
TTCTCTTGAT AAGAGACCAC TGGCCGTGGG CCGGTTCTGG ACAGTTTACA GAAGCTATGC 600
40 ACTTGATTGC CTTTGTGTCC CTGCTTCACC TTTTGAAGCA TAGGGCCCTA TTATAATGTA 660
TTTAAATGTG GTCTCCACCC CAAAGTGAAC ATGGGTTGCA TGTACAGGC ATGTTTACTC 720
AGCATGCATG CAGCAGGATC CCTTCACAAA TATTAGAGC TCCCCCTATT CCCTGTTGAA 780
TATGTATATG TGGCCAGCCA GATCAACGTA AATCACTATT CGCCCTCCCC TCCCTGGAAA 840
CCTACTTTTC GGGTTTCAGC AGGAAGCTAT GCCTCCAGG CTTGTGCAAG AGGGCCCRAT 900
45 TTCGGGCTTG ATAACCCCTT TATAAAAAAA TAAATCTCC TTTCTAAATT TAAATACAA 960
CCACACACCC GCGCCGCAAC TATTGGGGGG GAAAAAGAA GAAGACACAC GGTACATAGT 1020
TTCATGCACA TTGTTAAGGA GACAGGTGCC CCCAAGCAGG CGGACATCAC CAGTACGCA 1080
GCTTGAGCAT GCCGAAGACG CGAGCGACTC ATAGAACACG ACGACGCTCG CAAGGCACTA 1140
AGCATAGCTA CTACCACCTG TCGAAGAGTC ATACACAGAT TTCTATTGGC GA

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Seq ID NO: 23 DNA sequence
Nucleic Acid Accession #: CAT cluster

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1      11      21      31      41      51
|      |      |      |      |      |
55 CTATGAATCT CGGAAATTAC TCAAACCATC AGCCTCTGCA AGAAGCAAAG TGGACGGCCG 60
GGCCCGGTGG CTCACCTCTG GAATCCAGC ACTTTGGGAG CCCGAGGTGG CGGGATCAGC 120
AGGTCAGGAG ATCAGAGACTG TTCTGGCTAA ACCAGTGAAA CCCCCTCTCT ACTAAAAAAA 180
TAAGAAAAGC GAAGTGATC TCCATAAAC GAGGTACTGC AGGAAGAAAG CAGAAAATGA 240
GACCCAGATA CACACATGCA CGCGGCGGCC GCACACACAC ACCAGAAGAA ATGAACCAAG 300
60 AGGAAGAGAA ACATTTTCAA ATAAGCATTG GGAGATGGGA AAAACACCTT GAAACAGAAA 360
TTCATAAAGT ACAGAAATTT TTTTAACTT AAAAAAGGA CAATAATAGA CAGAAAATGA 420
ATGAAAAAAT AAATGTGATA TCAGAAATGA AGATAAATTA AAAGTGGTCA AAGGAGAAGA 480
GATCTAAATG CAAACTTAAG AAGGGGCAAT TTTTTTTTTT TTTTTTTTTT AGACGAGGCC 540
TCACTCTGTC GC

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Seq ID NO: 24 DNA sequence
Nucleic Acid Accession #: NM_000044.1
Coding sequence: 1115..3874

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1      11      21      31      41      51
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AGAGGAGGCG ACAGAGGGAA AAAGGGCCGA GCTAGCCGCT CCAGTGCTGT ACAGGAGCCG 120
AAGGGAGCGA CCAGCCAGC CCCAGCCCGG CTCAGCGCAG AGCCAACGCC TCTTCAGCG 180
75 CGGCGGCTTC GAAGCCCGCG CCCGAGCTG CCCTTTCTCT TTCGTSAGG TTTTAAAG 240
CTGCTAAAGA GCTTCAAGAA GCAAGGAAAG TGCCCTGGTAG GACTGACGGC TGCCCTTGTG 300
CTCTCTCTCT CCACCCCGCC TCCCCCAACC CTGCTTCCC CCCCCTCCCC GTCTTCTCTC 360
CCGCGAGTGC TCTAGTCGCG TACTCTCAGC CAACCCCTCT CACCAACCTT CTCCCCACCC 420
80 GCGCCCCCGC CCGCTCGGCG CCAGCGCTGC CAGCCCGAGT TTGCAAGAG GTAACTCCCT 480
TTGGCTGCGA GCGGGCGAGC TAGCTGCACA TTGCAAGAA GGCTCTTAGG AGCCAGGCGA 540
CTGGGAGCG GCTTCAAGCA TGCAGCCAG ACCCGCTGG TTAGAATTCC GCGGAGAGA 600
ACCTCTGTT TTCCCCCACT CTCTCTCCAC CTCTCTCTGC CTTCGCCACC CCGAGTGGCG 660
AGCAGACATC AAAAGATGAA AAGGCAGTCA GGTCTTCAGT AGCCAAAAAA CAAACAAAC 720

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AAAAACAAAA AAGCCGAAAT AAAAGAAAAA GATAATAACT CAGTTCTTAT TTGCACCTAC 780
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TTGTCCACCG TGTGTCTTCT TCTGCACGAG ACTTTGAGGC TGTACAGCGC CTTTTTGCCT 960
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GGGAAGTAGG TGAAGATTC AGCCAAGCTC AAGGATGGAA GTGCAGTTAG GGCTGGGAAG 1140
GGTCTACCTT CGGCCGCCGT CCAAGACCTA CCGAGGAGCT TTCCAGAATC TGTTCAGAG 1200
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GCAACTCCTT CAGCAACAGC AGCAGGAAGC AGTATCCGAA GGCAGCAGCA GCGGAGAGC 1740
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CATTTCTGAC AACGCCAAGG AGTTGTGTAA GGCAGTGTG GTGTCCATGG GCCTGGGTGT 1860
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ACTGCTACTC TTCAGCATTA TTCCAGTGA TGGGCTGAAA AATCAAAAAT TCTTTGATGA 3600
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Seq ID NO: 25 Protein sequence
Protein Accession #: NP_000035.1

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70
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Nucleic Acid Accession #: CAT cluster

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Seq ID NO: 28 Protein sequence
Protein Accession #: NP_006542.1

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50 ACCGAAAAA AAGCACAGGT TTATAACAAG CAGGATTATG ATCTCATGGT GTTTCCTGAA 240
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PCT/US02/17594

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WO 02/098358

PCT/US02/17594

Seq ID NO: 31 DNA sequence
Nucleic Acid Accession #: CAT cluster

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Seq ID NO: 34 DNA sequence
Nucleic Acid Accession #: CAT cluster

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PCT/US02/17594

Seq ID NO: 35 DNA sequence
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	CAGAAATATC	AGTTGAAAAA	GAGTACCAGT	GAGGCATATC	GAGGGCTGAG	TGCTTTCAGG	840
25	CTTTTGCGTT	TAGATCGCAA	CCATATTACC	TACGCTCCCC	AGGACAGTTT	TGAAGAGACT	900
	GTTCAGTTAC	GGCATCTGTG	CGTGGATGAC	AACAGCTTGA	CGGAGGTGCC	TGTGCACCCC	960
	CTCAGCAATC	TGCCCCACCT	ACAGSCGCTG	ACCCCTGGCT	TCAACMAGAT	CTCAAGCATC	1020
	CTCGACTTTG	CATTTACCAA	CTTTTCAAGC	CTGTAGTTTC	TGCATCTTCA	TAACAACATA	1080
	ATTAGAGGCC	TGAGTAAACA	CTGTTTGTAT	GACATAGATA	ACCTGGAGAC	CTTAGACTTG	1140
30	AGTTATAATA	ACTTTGGGGG	ATTTTCTCAG	GCTATTAAAG	CCCGTCTCAG	CTTTAAGAGT	1200
	CTAGGATTTT	ATAGTAATTC	TATTTCTGTT	ATCCTGATG	GAGACATTTG	TGGTAACTCA	1260
	CTCTTAAAGAA	CIATACATTT	GTATGATAAT	CTCTCTGCTT	TTGTGGGGAA	CTCAGCATCT	1320
	CACRAATTTT	CTGATCTTCA	TTCCCTAGTC	ATTCTGTGCT	CAGACATGTT	GCAGCACTTG	1380
35	CCCAATCTTA	CAGGAACGTG	CCACTGGGAA	AGTCTGAGT	TCAGACGGTC	AAAGATAAGG	1440
	AGCATACATA	ATAATTTGTG	TCAGAAGACAA	AAGATGCTTA	GGACATTTGA	CTTGTCTTAC	1500
	AATAATATTA	GAGACCTTCC	AAGTTTAAAT	GTTGTGCATG	CTCTGGAGA	AACTTCTTTA	1560
	CAGCGTAATC	AAATCTACCA	AATAAAGGAA	GGCACTTTC	AAGGCCTGAT	ATCTCTAAGG	1620
	ATTTCTAGATC	TGAGTAGAAA	CCTGATACAT	GAATATCACA	GTAGAGCTTT	TGCCACACTT	1680
40	GGGCCAATAA	CTAACCTAGA	CTAACGTTTC	ATAAGAACTA	TCTCCTTTC	TACGGGAAGC	1740
	CCGAATGGGC	TAAATCAACT	GAAACTTGTG	GGCAACTTCA	AGCTGAAAGC	AGSCCTTAGCA	1800
	GCAAAAGACT	TGTTTAACCT	CAGGCTTTTA	TCGGTACCAT	ATGCTTATCA	GTCGTGTGCA	1860
	TTTTGGGGTT	GIGACTCTTA	TGCAAAATTA	AACACAGAAG	ATAACAGCCT	CCAGSACCAC	1920
	AGTGTGACAT	AGGAGAAAGG	TACTGCTGAT	CGACCAAAAT	TCAACAGCAT	TCTTGAANAAT	1980
45	GAGAGACATA	GTCAAATAAT	TATCCATTGT	ACACCTTCAA	CAGGTGCTTT	TAAAGSCCTG	2040
	GAATATTTCA	TGGGAAGCTG	GATGATTCGT	CTTACTGTGT	GGTTCATTTT	CTTGGTTGCA	2100
	TTATTTTTCAC	ACCGCTCTGT	TATTTTAAAC	ACATTTGCAT	CTGTACATCT	ACTGCTCTTG	2160
	TCCAAATTGT	TTATAGGCTT	GATTTCTGTG	TCTAACTTAT	TCATGGGAAT	CTATACTGGC	2220
	ATCTTAACCT	TTCTTGATGC	TGTTGCTCTG	GGCAGATTGC	CTGAATTTGC	CTATTGGTGG	2280
50	GAAACTCGCA	TGGTCTGCAA	AGTAGCTGGT	TTTCTTGCAG	TTTCTCCTCT	AGAAATGTCG	2340
	ATATTTTAT	TGCTCTAGC	AACTGTGCAA	AGAGCTTCA	CTGCAAAAGA	TATAATGAAA	2400
	AATGGGGAAT	GCAATCATCT	CAAAACAGTA	CGGGTGTGCT	CCCTTTCGCG	TTTCTTAGGT	2460
	GCTACAGTAG	CAGGCTGTTT	TCCCTTTTTC	CATAGAGGGG	AATATTCTGC	ATCACCCCTT	2520
	TTTGTGCCAT	TTCTTACAGG	TGAAGACGCCA	CTATTAGGAT	TCACCTGTAAC	GTTAGTGCTA	2580
55	TGAAATCTAC	TAGCATTTTT	ATTAATGGCC	GTTATCTACA	CTAAGCTATA	CTGCAACTTG	2640
	GAAAAAGAGG	ACCTCTCAGA	AAACTCACAA	TTCAGCATGA	TAAAGCATGT	CGCTTGCTCA	2700
	ATCTTACACA	ATGTCAICTT	TTTCTGCCCT	GTTGGTGGCT	TTTCAATTGC	ACCAATTGATC	2760
	ACTGCAATCT	CTATCAGCCC	CGAAATAATG	AAGTCTGTTA	CTCTGATATT	TTTTCCATTG	2820
	CTCGCTTGCC	TGAATCCAGT	CTGTAATGTT	TTCTTCTAAC	CAAAAGTTTA	AGAAAGCTGG	2880
60	AAGTTACTGA	AGCCAGCTGT	TACCAAGAAAT	AGTGGATCAG	TTTCAGTTTG	CTCATGAGTA	2940
	CRAAGGTGTT	GTCGTGGAAC	GGATTTCTAC	TACGACTGTG	GCACTGATCT	ACATTTGSCG	3000
	GGCAACCTGA	GCTGTTGCGA	CTGCTGCGAA	TGCTTCTCTT			

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TAAAAATAGA AGAAGAAAGA ATAAAGCTTA GTCCTGTGTC TTTAAAAATT AAAAATTTTA 4500
CTTGATTCCTC ATCTATGGGC TTTAGACCTA TTACTGGGTC GAGTCTTAAA GTTATAATTG 4560
TTCAATATGT TTTTGAACA GTGTGCTAAA TCAATAGCAA ACCCACTGCC ATATTAGTTA 4620
TTCTGAATAT ACTAAAAAAA TCCAGCTAGA TTGCAGTTTA ATAATTAAAC TGTACATACT 4680
GTGCATATAA TGAATTTTAA TCTTATGTAA ATTATTTTAA GAACACAAGT TGGGAAATGT 4740
GGCTTCTGTT CATTTCTGTT AATTAAAGCT ACCTCCTAAA CTATAGTGGC TGCCAGTAGC 4800
AGACTGTAA ATTCTGGTT ATATACTTTT TCCATTGTAA ATAGTCTTTG TTGTACATTG 4860
TCAGTGTAA TAAAAACAGAA TCTTTGTATA TCAAAATCAT GTAGTTTGTG TAAATGTGG 4920
GAAGGATTAT TTACAGTGT GTTGTAAATT TGTAAAGCCA ACTATTTACA AGTTTAAAA 4980
ATTGCTATCA TGTATATTTA CACATCTGAT AAATATTAAA TCATAACTTG GTAAGAAACT 5040
CCTAATTAAA AGTTTATTTT CAAAATTTCAG GTTATTGAAA ATTTTTCATT TTATTCAATT 5100
AAAACTAGA ATAACAGATA TATAAAAGTG TTAATCTTTC TGCTATATGG TATGAANTAC 5160
AATATTGTAC TCAGTGTTTT GAATTATTAA AGTTTCTAGA AAGCAAAAAA A

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Seq ID NO: 36 Protein sequence
Protein Accession #: NP_060960.1

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1 11 21 31 41 51
MPGFLGLLGF LALGLLGSAG PSGAAPPLCA APCSCDGD RR VDCSGKGLTA VPEGLSAFTQ 60
ALDISMNNIT QLPEDAFKNF PFLEELQLAG NDLSFIHPKA LSGKLKELKVL TLQNNQLKTV 120
PSEAIRGLSA LQSLRLDANH ITSVPEDSFE GLVQLRHLWL DDNSLTEVPV HPLSNLPTLQ 180
ALTALNKSIS SIPDFAFTNL SSLVVLHLHN NKIRGLSQHC FDGLDNLLET L DLSYNNLGEF 240
PQAIKARPSL KELGFHSNSI SVIPDGA FDG NPLLRTHLY DNPLSFVGN SASHNLSDLHS 300
LVIRGASVMQ QFPNLTGT VH LESLTLTG TK ISSIPNNLCQ EQKMLRTL DL SYNNIRDLPS 360
FNGCHALBEI SLQRNIYQI KEGT PQQLIS LRILDLNRNL IHEIHSRAFA TLGPITNLDV 420
SFNELTSFPT EGNPNLNQK L LVGNFKLKEA LAAKDFVNL R SLSVPYAYQC CAFWGCDSYA 480
NLNTENDSLQ DHSVAGEKGT AADANVIST L ENEBHSQII HCTPSTGAFK PCEYLLGSWM 540
IRLTVMFIPL VALFFNLLVI LTTFASCTSL PSSKLFIGLI SVSNLFMGIY TGIPLTFLDAV 600
SWGRFAEPGI WWTGSGGCKV AGFLAVFSSE SAIFLLMLAT VERSLSAKDI MKNGKSNHLK 660
QFRVAALGAF LGATVAGCFP LFHRGEYSAS PLCLPFPPTGE TPSLGFTVT L VLLNSLAFLL 720
MAVIYTKLYC NLEKEDLSN SQSSMIKHVA WLIFTNCIFF CPVAFFSFAP LITAISSPE 780
IMKSVTLIFF PLPACLNPVL YVFFNPKFKE DWKLLKRRVT KKSQSVSVSI SSQGGCLEQD 840
FYDQCMYSH LQGNLTVDCD CESFLLTKPV SCKHLIKSHS CPALAVASCO RPEGYWSDCG 900
TQSAHSDYAD EEDSFVSDSS DQVQACGRAC FYQSRGFPLV RYXNLPVRK D

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Seq ID NO: 37 DNA sequence
Nucleic Acid Accession #: AF144648.1
Coding sequence: 1..1884

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1 11 21 31 41 51
ATGCTGCGAG CCGCAGTGAT CCTGCTGCTC ATCAGGACCT GGCTCGCGGA GGGCAACTAC 60
CCCGAGTCCA TCCCGAAAT CCACCTCGAG TTCTCCTCTG CTGTGCCCGA AGTCGTCTCT 120
AACCCTCTCA ACTGCAGAAA TTGTGCAAAAT GAAGCTGTGG TTCAAAAGAT TTTGGACAGG 180
GTGCTGTCAA GATACGATGT CCGCCTGAGA CCGAATTTTG GAGGTGCCCC TGTGCCTGTG 240
AGAAATATCA TTTATGTAC GAGCATTGAA CAGATCTCAG AAATGAATAT GGACTACACG 300
ATCAGCATGT TTTTTCATCA GACTTGGAAA GATTACGCT TAGCATACTA TGAGACCACC 360
CTGAAGTGA CCGTGGACTA TCGGATGCAT GAGAAGTTGT GGGTCCCTGA CTGCTACTTT 420
TTGAACAGCA CAGGTCTTT CGTGATGAT GTGACTGTGG AGAATCGCGT GTTTCAGCTT 480
CAGCCAGATG GAACGGTGG GTACGGCATC GACTCACCA CTACAGCAGC TTGTTCCTCT 540
GACITGCATA AATTCCTAT GGACAAGCAG GCCTGCAACC TGGTGGTAGA GAGCTATGGT 600
TACACGGTGT AAGACATCAT ATTATTCTGG GATGACAATG GGAACGCCAT CCACATGACT 660
GAGGAGCTGC ATATCCCTCA GTTCACTTTC CTGGGAAGGA CGATTACTAG CAAGGAGGTG 720
TATTTCTACA CAGGTTCCCTA CATACGCTG ATACTGAAGT TCCAGGTTC GAGGGAAGTT 780
AACAGCTACC TTTGTCAAGT CTACTGGCCT ACTGTCTCTA CCATATTAC CTCTTGGATA 840
TCGTTTGGG TGAACATGTA TTCTCTGCA GCCAGGGTGA CAATTGGCTT AACTTCAATG 900
CTCATCTTGA CCAACATCG CTACATCTG CGGGATAAGC TCCCCAACAT TTCCTGTATC 960
AAGGCCATG ATATCTATAT CCTCGTGTG TTGTTCTTTG TGTTCTCTGC CTGTCTGGAG 1020
TATGTCTACA TCAACTATCT TTTCTACAGT CGAGGACCTC GCGCCAGACC TAGGCGACAC 1080
AGGAGACCCC GAAGAGTCAT TGCCCGCTAC CGCTACCAGC AAGTGGTGGT AGGAAACCTG 1140
CAGGATGGCC TGATTAACTG GGAAGACGGA GTCAGCTCTC TCCCCTATCAG CCCAGCGCAG 1200
GCCCCCTGG CAAGCCCGGA AAGCCTCGGT TCTTTGACGT CCACCTCCGA GCAGGCCAGG 1260
CTGGCCACT CGGAAGCCT CAGCCCACTC ACTTCTCTCT CAGGCCAGGC CCCCTGGCC 1320
ACTGGAGAAA GCTTGAGCGA TCTCCCTCC ACCTCAGAGC AGGCCCGGCA CAGCTATGGT 1380
GTTGCTTTTA ATGGTTTCCA GGCTGATGAC AGTATTTTTC CTACCGAAAT CCGCAACCGT 1440
GTGCAAGCCC ATGGCCATG TGTATCCCAT GACCATGAAG ATTCCAATGA GAGCTTGAGC 1500
TCGGATGAGC GCCATGGCCA TGGCCCCAGT GGGGAAGCCA TGCTTACCA TGGCGAGAAG 1560
GGTGTGCAAG AAGCAGGCTG GGACCTTGAT GACAACAATG ACAAGAGCGA CTGCCTTGCC 1620
ATTAAGGAGC AATTCAAGTG TGATACTAAC AGTACCTGGG GCCTTAATGA TGATGAGCTC 1680
ATGGCCCATG GCCAAGAGAA GGACAGTAGC TCAGAGTCTG AGGATAGTTG CCCCCAAGC 1740
CCTGGTGTCT CCTTCACTGA AGGGTTCTCC TTCGATCTCT TTAATCTCTG CTACGTCCCA 1800
AAGGTCGACA AGTGGTCCCG GTTCTCTTTC CCTCTGGCCT TTGGGTTGTT CAACATTGTT 1860
TACTGGGTAT ACCATATGTA TTAG

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Seq ID NO: 38 Protein sequence
Protein Accession #: AAD51172.1

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1 11 21 31 41 51
MLRAAVILL IRTWLAEGNY PSPIPKFHF FSSAVPEVVL NLFNCKNCAN EAVVQKILDR 60
VLSRYDVR LR PNFGGAPVEV RISIYVTSIE QISEMNM DY ITMFFHQYWK DSRLAYYETT 120
LNLTLDRMH EKLWVPDCYF LNSKDAFVHD VTVENRVFQL HPDGTVRVYK RLTTAAACSL 180

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PCT/US02/17594

5 DLHKPMDKQ ACNLVVESYG YTVEDIILFW DDNGNAIHMT EELHIPQFTF LGRTITSKEV 240
YFYTGSIYRL ILKQVQREV NSYLVQVYWP TVLTITTSWI SFWMNYDSSA ARVTIGLTSM 300
LILTTIDSHL RDKLPNISC KAIIDYILVC LFFVFLSLE YVINYLFYS RGP RRQPRRH 360
RRRRRIARY RYQVVVGNV QDGLINVEDG VSSLPTPAQ APLASPELGD SLTSTSEQAQ 420
LATSESLSP TSLSGQAPLA TGESLSDLP TSEQARHSYG VRFNGFQADD SIFPTEIRNR 480
VEAHGHGVTH DHEDSNESLS GDERHGHGPG GKPLMLHGEK GVQEGAWDL DNNKSDCLA 540
IKEQFKCDTN STWGLNDEL MAHQEKDSS SESEDS CPPS PGCSFTEGFS FDLFNPDYVP 600
KVDKWSRFLF PLAFGLFNIV YWVYHMY

10 Seq ID NO: 39 DNA sequence
Nucleic Acid Accession #: U47334.1
Coding sequence: 1..331

15 1 11 21 31 41 51
CAAAAATTGT GCAAAATGAAG CTGTGGTTCA AAAGATTTTG GACAGGGTGC TGTCAGATA 60
CGATGTCCGC CTGAGACCGA ATTTTGGANN NATGCTTGCT ACTAACAGTA CCCGGGGCCT 120
TAATGAAGAT GAGCTCATGG CCCATGGCCA AGAGAAGGAC AGTAGCTCAG AGTCTGAGGA 180
TAGTTGCCCC CCAAGCCCTG GGTGCTCCTT CACTGAAGGG TTCTCCTCG ATCTCCTTAA 240
20 TCCTGACTAC GTCCCAAAG TCGACAAAGT GTCCCGGTTT CTCTTCCCTC TGCCCTTTGG 300
GTTGTTCAAC ATTTAGTCGG CCGAACGATG C

25 Seq ID NO: 40 Protein sequence
Protein Accession #: AAC50559.1

1 11 21 31 41 51
KNCANEAVVQ KILDRVLSRY DVRLRPNFGX MLATNSTRGL NEDELMAHQG EKDSSESESD 60
30 SCPPSPGCSF TEGFSFDLLN PDYVPKVDKW SRFLEPLAFG LFNIVAAERC

Seq ID NO: 41 DNA sequence
Nucleic Acid Accession #: NM_020974
Coding sequence: 81..3080

35 1 11 21 31 41 51
GGCGTCCGG CACACCTCCC CGCGCCGCG CCGCCACCG CCGCACTCCG CCGCCTCTGC 60
CCGCAACCGC TGAGCCATCC ATGGGGGTCG CGGGCCGCAA CGTCCCCTGG CCGGCTCTGG 120
CGGTGCTGCT GCTGCTGCTG CTGCTGCCGC CACTGCTGCT GCTGGCCGGG CCGCTCCCGC 180
40 CGGTGCGGG CGGTGCCGGG GGGCCGCGAG AGGATGTAGA TGAGTGTGCC CAAGGGCTAG 240
ATGACTGCCA TGCCGACGCC CTGTGT CAGA ACACACCCAC CTCCTACAAG TGCTCCTGCA 300
AGCTGGCTG CCAAGCGGAA GCGAGGCAGT GTGAGGCAT CGATGAATGT GGAAATGAGC 360
TCRAATGAGG CTGTGTCCAT GACTGTGTTGA ATATTCCAG CAATTATCGT TGCACCTGTT 420
45 TTGATGGCTT CATGTGGCTT CATGACGGTC ATAATTGTCT TGATGTGAC GAGTGCCTGG 480
AGAACATAG CGGTGCGGAG CATACCTGTG TCAACGTCAT GGGGAGCTAT GAGTGTGCT 540
GCAAGAGAGG GTTTTTCCTG AGTGACAATC AGCACACCTG CATTACCCGC TCGGAAGAGG 600
GCCTGAGCTG CATGAATAAG GATCACGGCT GTAGTCACAT CTGCAAGGAG GCCCAAGGG 660
GCAAGCTGCG CTGTGAGTGC AGGCTGTGTT TTGAGCTGGC CAAGAACCAG AGAGACTGCA 720
TCTTGACCTG TAACCATGGG AACGGTGGGT GCCAGCACTC CTGTGACGAT ACAGCCGATG 780
50 GCCCAGAGTG CAGCTGCCAT CCACAGTACA AGATGCACAC AGATGGGAGG AGCTGCCTTG 840
AGCGAGAGGA CACTGTCTCT GAGGTGACAG AGAGCAACAC CACATCAGTG GTGGATGGGG 900
ATAAAGCGGT GAAACGGCGG CTGCTCATGG AAACGTGTGC TGTCAACAAT GGAGGCTGTG 960
ACCGCACCTG TAAGGATACT TCGACAGGTG TCCACTGCAG TTGTCTGTGT GGATCACTC 1020
TCCAGTTGGA TGGGAAGACA TGTAAGATA TTGATGAGTG CCAGACCCGC AATGGAGGTT 1080
55 GTGATCAATT CTGCAAAAC ATCGTGGGCA GTTTGACTG CGGCTGCAAG AAAGGATTTA 1140
AATTATTAAC AGATGAGAAG TCTTGCCAAG ATGTGGATGA GTGCTCTTTG GATAGGACCT 1200
GTGACCACAG CTGCATCAAC CACCCTGGCA CATTTGCTTG TGCTTGCAAC CGAGGGTACA 1260
CCCTGTATGG CTTCAACCCAC TGTGGAGACA CCAATGAGTG CAGCATCAAC AACGGAGGCT 1320
60 GTCAGCAGGT CTGTGTGAAC ACAGTGGGCA GCTATGAAT CCAGTGCCAC CCTGGGTACA 1380
AGCTCCACTG GAATAAAAAA GACTGTGTGG AAGTGAAGGG GCTCCTGCCC ACAAGTGTGT 1440
CACCCTGTGT GTCCCTGCAC TGCCTTAAGA GTGGTGGAGG AGACGGGTGC TTCTCAGAT 1500
GTCACTCTGG CATTCACTCT TCTTCAGATG TCACCACCAT CAGGACAAGT GTAACCTTTA 1560
AGCTAAATGA AGGCAAGTGT AGTTTGAATA ATGCTGAGCT GTTCCCGAG GGTCTGCGAC 1620
CAGCACTACC AGAGAAGCAC AGCTCAGTAA AAGAGAGCTT CCGCTACGTA AACCTTACAT 1680
65 GCACTCTGG CAAGCAAGTC CCAGGAGCCC CTGGCCGACC AAGCACCCCT AAGGAAATGT 1740
TTATCACTGT TGAGTTTGA CTTGAAACTA ACCAAAAGSA GGTGACAGCT TCTTGTGACC 1800
TGAGCTGCAT CGTAAAGCGA ACCGAGAAGC GGCTCCGTAA AGCCATCCGC ACGCTCAGAA 1860
AGGCCGTCCA CAGGGAGCAC TTTCACTCC AGCTCTCAGG CATGAACCTC GACGTGGCTA 1920
70 AAAGCCTCC CAGAACATCT GAACGCCAGG CAGAGTCTTG TGGAGTGGGC CAGGGTCAATG 1980
CAGAAAACCA ATGTGTGAGT TGCAGGGCTG GGACCTATTA TGATGGAGCA CGAGAACGCT 2040
GCATTTTATG TCCAAATGGA ACCTTCCAAA ATGAGGAAGG ACAAATGACT TGTGAACCAT 2100
GCCCAAGACC AGGAATTTCT GGGGCCCTGA AGACCCGAGA AGCTTGGAAT ATGTCTGAAT 2160
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75 GTGCCCTGG CACGTTCCAG CTTGAAGCTG GTGCAACTTC CTGCTTCCCC TGTGAGGAG 2280
GCCTTGCCAC CAACATCAG GGAGCTACTT CCTTTCAGGA CTGTGAAACC AGAGTTCAAT 2340
GTTCACTGG ACATTTCTAC AACCCACCA CTCACCGATG TATTCTGTGC CCACTGGGAA 2400
CATACAGCC TGAATTTGGA AAAAATAATT GTGTTCTTG CCCAGGAAAT ACTACGACTG 2460
ACTTTGATG CTCACCAAAC ATAACCCAGT GTAAAAACAG AAGATGTGGA GGGGAGCTGG 2520
80 GAGATTTCAC TGGGTACATT GAATCCCAA ACTACCCAGG CAATTACCCA GCCAACACCG 2580
AGTGTACGTG GACCATCAAC CCACCCCCCA AGCGCCGAT CCTGATCGTG GTCCCTGAGA 2640
TCTTCTGCT CTTCAAGGAG GACTGTGGGG ACTATCTGGT GATGCGGAAA ACCTCTTCAT 2700
CCAATTCTCT GACAACATAT GAAACCTGCC AGACCTACGA ACGCCCATC GCCTTCACCT 2760
CCAGGTCAAA GAAGCTGTGG ATTCAGTTCA AGTCCAATGA AGGGAACAGC GCTAGAGGT 2820

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TCCAGGTCCC ATACGTGACA TATGATGAGG ACTACCAGGA ACTCATTGAA GACATAGTTC 2880
GAGATGGCAG GCTCTATGCA TCTGAGAAAC ATCAGGAAAT ACTTAAGGAT AAGAAACTTA 2940
TCAAGGCTCT GTTGTAGTGC CTGGCCCATC CCCAGAACTA TTTCAAGTAC ACAGCCCAGG 3000
AGTCCCGAGA CATGTTTCCA AGATCGTTCA TCCGATTGCT ACGTTCCAAA GTGTCCAGGT 3060
TTTGTAGACC TTACAAATGA CTCAGCCAC GTGCCACTCA ATACAAATGT TGTGCTATAG 3120
GGTTGGTGGG ACAGAGCTGT CTTCCTTCTG CATGTGAGCA CAGTCGGGTA TTGCTGCCTC 3180
CCGTATCAGT GACTCATTAG AGTTCAATTT TTATAGATAA TACAGATATT TTGTTAAATT 3240
GAACCTGGTT TTTCTTTCCC AGCATCGTGG ATGTAGACTG AGAATGGCTT TGAGTGGCAT 3300
CAGCTTCTCA CTGCTGTGGG CGGATGTCTT GGATAGATCA CGGGCTGGCT GAGCTGGACT 3360
TTGGTCAGCC TAGGTGAGAC TCACCTGTCC TTCTGGGGTC TTACTCTCC TCAAGGAGTC 3420
TGTAAGTGAAG AGGAGGCCAC AGAATAAGCT GCTTATTCTG AAACITCAGC TTCTCTAGC 3480
CCGGCCCTCT CTAAGGGAGC CCTCTGCACT CGTGTGCAGG CTCTGACCAG GCAGAACAGG 3540
CAAGAGGGGA GGAAGGAGA CCCCTGCAGG CTCCCTCCAC CCACCTTGAG ACCTGGGAGG 3600
ACTCAGTTTC TCCACAGCCT TCTCCAGCCT GTGTGATACA AGTTTGATCC CAGGAACCTG 3660
AGTTCTAAGC AGTGCTCGTG AAAAAAAGAA GCAGAAAGAA TTAGAAATAA ATAAAACTA 3720
AGCACTTCTG GAGACAT

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Seq ID NO: 42 Protein sequence
Protein Accession #: NP_066025

1 11 21 31 41 51
MGVAGNRNRP AAWAVLLLLL LPPPLLLLAG AVPPGRGRGA GPQEDVDECA QGLDDCHADA 60
LQMTTPSYK CSCRPYQGE GRQCEIDDEC GNELNGGCVH DCLNIPGNRY CTCPDGFMLA 120
25 HDGHNCLDVD ECLENNNGGQ HTCVNVMGSY ECCCKEGFLL SDNQHTCIHR SEEGLSMKNK 180
DHGCSHICKE APRGSVACBC RPFELAKNQ RDCILTCHNG NGGQCHSCDD TADGPECSCH 240
PQYKMTDGR SCLEREDTVL EVTESNTTSV VDGDKRVKRR LLMETCAVMN GGCDRTCKDT 300
STGVHSCSPV GFTLQLDGKT CKDIDECQTR NGGCDHFCKN IVGSFDCGCK KGFKLLTDEK 360
SQQDVDECSL RDTDCSHSCN HPGTFAACAN RGYTLVGFTH CGDNECSIN NGGQQVVCVN 420
30 TVGSYECQCH PRYKHLWNKK DCVEVKGLLP TSVSPRVSLH CGKSGGGDGC FLRCHSGIHL 480
SSDVTITRTS VTFKLNEGKC SLKNABLEPE GLRPALPEKH SSVKESPRYV NLTCSSGKQV 540
PGAPGRPSTP KEMFITVEFE LETNQKEVTA SCDLSCIVKR TEKRLRKAIR TLRKAVHREQ 600
FHLQLSGMML DVAKKPRTS ERQABSCGVG QGHAEQCVS CRAQTYVDGA RERCILCPNG 660
TFQNEBQMT CEPCPRPGNS GALKTPAWN MSECGLCQP GEYSADGFAP CQLCALGTFQ 720
35 PEAGRTSCFP CGGLATKHQ GATSFQDCET RVQCSPPGHFY NTHHRCIR FVGTYPQBEF 780
KNNCVSCPN TTTDFDSTN ITQCKNRRCG GBLGDFGTGI BSEPNYPGNYP ANTECTWTIN 840
PPPKRRLIV VPEIFLPIED DCGDYLVMRK TSSSNSVTY ETCQTYERPI APTSRSKKLW 900
IQPKSNEGNS ARGQVQVYV YDEDYQLIE DIVRDGRLYA SENHQEILKD KKLKALFEDV 960
40 LAHPQNYFKY TAQESREMPF RSFIRLLRSK VSRFLRPYK

45

Seq ID NO: 43 DNA sequence
Nucleic Acid Accession #: CAT cluster

1 11 21 31 41 51
TTTCTTCATT TTAGCTTTT CTCCCTTTA TATATACTGG GCGGTTTTC CTGAGAAAT 60
TTTCCATCTC ATTAATCTCT CTGCAGCAAT TCATAACTCT TTGGGGGCAT TCCTTTGTTT 120
TTTGATATGA CTACTACCTG ACTGTATATA GTTTCCTTTT TTTTTTTTTC CTCCAGATT 180
CTCTCTTTTC TACTGGCATC CTTTTCATT TTAACAATT TTCTCAGTT AGGTGACTT 240
50 GCITTTATAC CTGTGTGATG CTCTTGCCA GATATCTAGC AAATGCCCCC AGGATCCAAT 300
CAITTTTTC CTAAGAAAC TGAAAGAAAG CATGGCAAT AACAGAGCTT GGAATAAGG 360
AACTTTTAAA ATACAAACCC CAGTGAATC TACTTGAAG CCAATGCTTA GAGCAACAG 420
ACAGTGATTC AAATAGGTGT TGANNNNNNN NNNNNNNNN NATGATCAGC ATAGCAAAGA 480
TCACCTTCCA ACATTGGAAA GTTATGCATA TTCCAATTGA GCTAGCCCTT TTAACAGCC 540
55 TTAATAATTG ATAAAGAGA AGAAATTAA GATATTGAAA ACTGGTAGAT AATAAAACCT 600
AAATAAGCT GGTTTTGAA GAGCAGTGGC CACTGTGATT GACAAATGGG GCACTTACTG 660
TTAAGGGGAT TTAACAGA AGTACTTCAA CAGAATTGTG AAGAGAATAG AATTGTGAT 720
TCTTTTATCT GCCCAGAAC ACAGCTCCCA TGGGAAATAC TCCACCTCAT TCTACACCT 780
TCTGGCTGCA ACAAAGCAG TCAATTAATA ACATAACCCA AAGGGGTAC CTAACCAAC 840
60 TTGAGAAAT CATAGCAATC TCCCTTGGC TATAACTNTT TCCACATGAA ATACATTCAA 900
ATGCCCT

65

Seq ID NO: 44 DNA sequence
Nucleic Acid Accession #: CAT cluster

1 11 21 31 41 51
TTTTTTTTTT TTTTGTGGA TTTAGTATG CCTTGCAATT TTTTCCCTTT ATTCTGATGC 60
ATGAAGTACC CACTAAAAGT GACTGCTGTT AGTATAGCTT CAGTAATGAG GTGATGAGGT 120
70 GACAGGGCAG GTGATGCTCT CTTAGTCTCT TTAGGCTACT ATTACAAAT ACTTCAGACT 180
GACTAATTCA TAAACAACAG AGATTATTGT TCACAGATCT GGAGGCTGGA AAGTACAAGA 240
CTAAAGGGCC AGAATATTG GTGTTTGGTG AAGGTCAAAC ATTCAGACAC TCTCAACGAC 300
TATAGCGACA GCAGCATCT TCAGGAATCC TATGTGAGGG ACAAACTC AGAAGCCAGC 360
TGGAGGTGTC TAGAATCCTA TGTGAGGGAC AAACATTGAG ACCCCAGCAG TAGTGTGTG 420
75 GARTCCATAG TGAGGGACAA ACTTTCAAC CTTGTAGCA GTGTCTGGA ATCTATGTG 480
AGGGACAAA ATTCAAGC TTGTAGCAGT GTTCTGGAAT CCTATGTGAG GAACATCA

80

Seq ID NO: 45 DNA sequence
Nucleic Acid Accession #: Bos sequence
Coding sequence: 31..1092

1 11 21 31 41 51
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AAACACCACT AGGAAACAAT ACATATGAG ACCCAGCAGA AGCAACAGAT TGACTCTAGA
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Seq ID NO: 46 Protein sequence
Protein Accession #: Eos sequence

1 11 21 31 41 51
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TGGEVDVRAG QGPEEDGGR ARLAQAAASS SPRHRATSCT LGSSRPSSRG LPAAPKSALA 120
LLWPRRWRSS CTRCSCCWYQ SRPRALISKP CSSTSFSCSS SFICFSRPQS TPLAMVCLRR 180
SPRARGARRA SPESAPGPGT PLHRDKHEAL SLQTRRGALQ DPBSTKSRSP VPSLRPRWSS 240
VPAPRSSTAR APRGRAPPQP GRTAAPGCGR RRWDREGRA RPAGASSEF PSAARPERPT 300
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Seq ID NO: 47 DNA sequence
Nucleic Acid Accession #: NM_020957.1
Coding sequence: 1156..3486

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AGTAGGAAGT AGAGTTAACC TATAGTTTCA TTCTTGAAT TTCTATTCT CTTTCTTCAG 180

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 TGTTTGGGAA TGAATTTTCC AATAACTTGA AAGTTGTAAA AACTCACACT TCTCAGGGTT 480
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80 Seq ID NO: 48 Protein sequence
 Protein Accession #: NP_066008.1

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LRVIDINDHS	PMFTEKEMIL	KIPENSPLGT	EPFLNHALDL	DVGSMNVONY	KISPSHFVR	180
LIHEFRDGRK	YPBELVDKEL	DREEEPQLRL	TLTALDGGSP	PRSGTAQVRI	EVVDINDNAP	240
EFEQPIYKVQ	IPENSPLGSL	VATVSARDLD	GGANGKISYT	LFQPSBEDISK	TLEVNPMTGE	300
VRLRKQVDFE	MVTSYEVRIK	ATDGGGLSGK	CTLLQLQVVDV	NDNPQVQVMS	ALTSFIPENS	360
PEIVVAVFSV	SDPDSGNNGK	TISSIQEDLP	FLKPSVKNF	YTLVTERALD	REARAEYNIT	420
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GTNAQVTVSL	LPQDPHLFL	ASLVSINADN	CHLFLRLSLD	YEALREFEFR	VSATDRGSPA	540
LSSEALVRVL	VLDANDNSPF	VLYPLQNGSA	PCTBLVPRAA	EPGYLVTKVU	AVDGDGSGNA	600
WLSYQLLKAT	EPGLFGVWAH	NGEVRTARLL	SERDAAKQRL	VVLVKDNGEP	PRSATATLHV	660
LLVDGFSQPF	LPLPEAAPQQ	TQANSLTVYL	VVALASVSSL	FLFSVLLFVA	VRLCRRESRAA	720
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Seq ID NO: 49 DNA sequence
Nucleic Acid Accession #: CAT cluster

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TATACTAAAT	AAAGAAATAA	CAGGAATAG	AAATGAAGA	AGAAAACAIT	AGCTATTGTC	240
AAACCAATAA	AAATTTGTGA	ATCTCTAAGC	ACATGAACCT	TGTATTATTT	GTACAGCATG	300
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Seq ID NO: 50 DNA sequence
Nucleic Acid Accession #: AF034799.1
Coding sequence: 170..3943

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CTCGACTCA	AGTCCCATTT	TTGAGCAGCT	GATCGTGAAT	ATGCTAGATG	AAAGGGATCG	300
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CGATGCCAG	ACGCTAGACC	TGATGCTTCA	GGAACRAATT	GATGCCATCA	ACAAAGAAAT	2160
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TGAAGAAATG GAAATCTTG CAGCTCCAGC AAAAACGAAA GAATCTGAGG AAGGAAGCTG 3180
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TGGAAATGAA TGGCTTCCCA GCTTGGGGTT ACCTCAGTAC AGAAGTTACT TTATGGAATG 3300
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AATGGTGGAT AGTTTCCATC GAACAAGTTT ACAATATGGA ATTATGTGCT TAAAGAGGTT 3420
10 GAATTTATGAC AGAAAGAAGC TAGAAAGAAG ACGGGAAGCA AGCCAAACATG AAATAAAGA 3480
CGTGTGGTGT TGGAGCAATG ACCGAGTTAT TCGCTGGATA CAAGCAATTG GACTTCGAGA 3540
ATATGCAAAAT AATATACCTG ACAGCGGTGT GCATGGCTCA CTTATAGCCC TGGATGAAAA 3600
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GCAAGTCTT GAAAGAGAA ACAATAACCT CTTGGCCCTG GGAAGTGAAG GCGACTGGA 3720
15 TGAAGTGAT GACAAGAACT TCAGACCTGG ATCAACCTGG AGAAGGCACT TTCTCCTCG 3780
TGAAGTACAT GGAATCAGCA TGATGCTTGG GTCTCAGAA ACATTACCAG CTGGATTTAG 3840
GTTAACCACA ACCTCTGGGC AGTCAAGAAA AATGACAACA GATGTGTGCTT CATCAAGACT 3900
GCAGAGCTTA CACAACCTCA CTGTTCCGAC ATACTCATGT TGACCAGCCA CTCGAAGGAG 3960
20 GCAGCACTGA CCTGCTATGG CGTCTTTTCA GTCTACTCTA CCTAAAGTGC ACTACCATCT 4020
AAGAAGACGA GCACTGAAAA CCTTTGTGAA AACTGAATTC

Seq ID NO: 51 Protein sequence
Protein Accession #: AAC26100.1

25 1 11 21 31 41 51
| | | | | |
MMCEVMPTIN EDTFMSQRGS QSSGSDSDSH FEQLMVNMLD ERDRLLDTLR ETQESLSLAQ 60
QRLQDVIYDR DSLQRLQNSA LPQDIESLTG GLAGSKGADP PEFAALTKEB NACREQLLEK 120
30 BEBISBELKAE RNNRLLEH LECVSRHER SLRMTVVKQK AQSPSGVSSE VEVLKALKSL 180
FEHKKALDEK VRERLRVSLR RVSALEBELA AANQEIVALK EQNVHIQRKM ASSEGSTESE 240
HLBGMPEPGK VHEKRLSNGS IDSTDETSQI VELQELLEKQ NYEMAQMKER LAALGSRVGE 300
VEQEAETARK DLIKTEEMNT KYQRDIREAM AQKEDMEERI TTLEKRYLSA QRESTSIHDM 360
NDRKLENELAN KEAILRQMBE KNRQLQERLE LAEEKLQQTM RKAETLPEVE ABLAQRIAL 420
35 TKABETHGNI EERMRLHGGQ LEEKNQBLQR ARQREKMBEE HNKRLSDTVD RLLTESNERL 480
QLHLKERMAA LEEKNLVIEQ SETFRKNLEE SLHDKESLAE EIEKLRSELD QLKMRGTSLI 540
EPTIPRTHLD TSAELRYSVG SLVDSQSDYR TTKVIRRPFR GRMGVRRDEP KVKSLGDHEW 600
NRTQQIGVLS SHPFESDTEM SDIDDDRET IFSSMDLLSP SGHSDAQTLA MMLQBLDAI 660
40 NKEIRLIQEE KESTELRABE IENRVASVSL EGLNLAMVHP GTSITASVTA SSLASSSPPS 720
GHSTPKLTPR SPAREMDRMG VMTLPSDLRK HRRKIAVVEE DGREDKATIK CETSPPPTPR 780
ALRMHTLPS SYHNDARSSL SVSLEPESLG LGSANSSQDS LHKAPKKGI KSSIGRLFGK 840
KEKARLQQLR GFMEETAAAG ESLGLGLGT QAEKDRRLKK KHELLEEARR KGLPFAQWDG 900
PTTVAVLBLEW LGMPAWYVAA CRANVKSGAI MGALSDTEIQ RBIGISNPLH RLKRLAIQE 960
MVSLSLSPSAP FTSRTPSGNV WVTHEEMENL AAPAKTKESE EGSWAQCPVF LQTLAYGDMN 1020
45 HEWIGNEWLF SLGLPQYRSY FMECLVDARM LDHLTKKDLR VHLKMVDSFH RTSLOYGIMC 1080
LKRLNYDRKE LBRREASQH BIKDVLVWSN DRVIRWIAI GLREYANNIL ESOVHGSLIA 1140
LDENFDYSSL ALLLIPTQIN TQARQILERE YNNLLALGTE RRLDESDDKN FRRGSTWRRQ 1200
PPPREVHGIS MMPGSSETLP AGFRLTTTSG QSRKMTTDVA SSRQLRLDNS TVRTYSC

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It is understood that the examples described above in no way serve to limit the true scope of this invention, but rather are presented for illustrative purposes. All publications, sequences of accession numbers, and patent applications cited in this specification are herein
5 incorporated by reference as if each individual publication or patent application were specifically and individually indicated to be incorporated by reference.

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WHAT IS CLAIMED IS:

1. A method of detecting an androgen-independent prostate cancer cell in a sample from a patient having undergone androgen ablation therapy, the method comprising determining the presence or absence of a nucleic acid comprising a sequence at least 80% identical to a sequence as shown in Tables 1A-4.
- 5 2. The method of claim 1, wherein said determining is by hybridizing with a polynucleotide that selectively hybridizes to a sequence at least 95% identical to a sequence as shown in Tables 1A-4.
- 10 3. The method of claim 1, wherein the biological sample:
 - a) is a tissue sample; or
 - b) comprises isolated nucleic acids.
- 15 4. The method of claim 3:
 - a) wherein the nucleic acids are mRNA; or
 - b) further comprising the step of amplifying nucleic acids before the step of contacting the biological sample with the polynucleotide.
- 20 5. The method of claim 2, wherein the polynucleotide:
 - a) comprises a sequence as shown in Tables 1A-4;
 - b) is labeled, including a fluorescent label; or
 - c) is immobilized on a solid surface.
- 25 6. The method according to claim 1, wherein said biological sample is contacted with a plurality of polynucleotides that each selectively hybridizes to a sequence at least 95% identical to a first sequence as shown in Tables 1A-4.
- 30 7. The method according to claim 6, wherein said plurality of polynucleotides are immobilized on a solid surface.

8. An isolated polypeptide which is encoded by a nucleic acid molecule having polynucleotide sequence as shown in Tables 1A-4.
9. An antibody that specifically binds a polypeptide of claim 8.
- 35 10. The antibody of claim 9:
- a) further conjugated to an effector component, including a fluorescent label a radioisotope or a cytotoxic chemical; or
- b) which is an antibody fragment or humanized antibody.
- 40 11. A method of detecting an androgen-independent prostate cancer cell in a patient having undergone androgen ablation therapy, the method comprising contacting a sample from said patient with an antibody of claim 9.
- 45 12. The method of claim 11, wherein:
- a) the antibody is further conjugated to an effector component, e.g., a fluorescent label; or
- b) said sample comprises a cell.
- 50 13. A method of detecting antibodies specific to androgen-independent prostate cancer in a patient having undergone androgen ablation, the method comprising contacting a biological sample from the patient with a polypeptide encoded by a nucleic acid comprising a sequence from Tables 1A-4.
- 55 14. A method of inhibiting proliferation of androgen-independent prostate cancer cells in a patient having undergone androgen ablation therapy, the method comprising administering to the patient a therapeutically effective amount of a compound that specifically eliminates cells expressing an antigen listed in Tables 1A-4.
- 60 15. The method of claim 14, wherein the compound is an antibody.
16. A drug screening assay comprising the steps of:

- a) administering a test compound to a mammal having a prostate proliferative condition or a cell isolated therefrom;
- 65 b) comparing the level of gene expression of a polynucleotide that selectively hybridizes to a sequence at least 80% identical to a sequence as shown in Tables 1A-4 in a treated cell or mammal with the level of gene expression of the polynucleotide in a control cell or mammal, wherein a test compound that modulates the level of expression of the polynucleotide is a candidate for the
- 70 treatment of prostate cancer.
17. The assay of claim 16, wherein:
- a) the control is a mammal with prostate cancer or a cell therefrom that has not been treated with the test compound; or
- 75 b) the control is a normal cell or mammal.
18. A method for treating a mammal having a prostate proliferative condition or prostate cancer comprising administering a compound identified by the assay of claim 16.
- 80 19. A pharmaceutical composition for treating a mammal having a prostate proliferative condition or prostate cancer, the composition comprising a compound identified by the assay of claim 16 and a physiologically acceptable excipient.
20. A method of detecting a prostate cancer associated transcript, the method comprising
- 85 contacting a biological sample from the patient with a plurality of polynucleotides wherein at least two of said polynucleotides selectively hybridize to a difference sequence at least 80% identical to a sequence as shown in Tables 1A-4.
21. A method of detecting a prostate cancer, the method comprising the steps of:
- 90 a) providing a biological sample from a patient;
- b) contacting the biological sample with a first polynucleotide that selectively hybridizes to a sequence at least 80% identical to a first sequence as shown in Tables 1A-4, to determine the level of a prostate cancer-associated transcript in the biological sample; and with a second polynucleotide that selectively

95 hybridizes to a second sequence at least 80% identical to a sequence not
 shown in Tables 1A-4; wherein the expression of said second sequence is not
 substantially changed in prostate cancer, to determine the level of expression
 of a control transcript in the biological sample; and
 c) comparing the level of the prostate cancer-associated transcript to a level of the
100 normal tissue associated transcript in the biological sample.

22. A method for quantitation of a prostate cancer-associated transcript in a cell from a
patient, the method comprising contacting a biological sample from the patient with a
polynucleotide that selectively hybridizes to a sequence at least 80% identical to a sequence
105 as shown in Tables 1A-4.

23. The method of claim 22, wherein:
 a) the polynucleotide selectively hybridizes to a sequence at least 95% identical to a
 sequence as shown in Tables 1A-4;
110 b) the biological sample is a tissue sample;
 c) the biological sample comprises isolated nucleic acids;
 d) the nucleic acids are mRNA;
 e) further comprising the step of amplifying nucleic acids before the step of
 contacting the biological sample with the polynucleotide;
115 f) the polynucleotide comprises a sequence as shown in Tables 1A-4;
 g) the polynucleotide is labeled, including a fluorescent label; or
 h) the polynucleotide is immobilized on a solid surface.

24. A biochip comprising a plurality of polynucleotides that selectively hybridize to a
120 sequence at least 80% identical to a sequence as shown in Tables 1A-4.

25. A method of screening drug candidates comprising:
 a) providing a cell that expresses an expression profile gene selected from the group
 consisting of an expression profile gene set forth in Tables 1A-4 or fragment
125 thereof;
 b) adding a drug candidate to said cell; and

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- c) determining the effect of said drug candidate on the expression of said expression profile gene.

- 130 26. A method according to claim 22 wherein said determining comprises comparing the level of expression in the absence of said drug candidate to the level of expression in the presence of said drug candidate.